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ROUND-TABLE CONFERENCE ON THE DISORDERS OF MENSTRUATION[1]

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DR. COSBIE: The disorders of menstruation are, of course, an important subject to the practitioner, not only because he has these problems frequently to solve, but because these disorders, often the evidence of trifling functional disturbance, may be the signs of serious organic disease. The duty of the physician, when confronted with these problems, is one which concerns itself wherever possible with the conservation and efficient function of the reproductive organs, and it is in this field that judgment is both difficult and of the utmost importance to the patient. Only on a proper consideration of the underlying physiology and pathology of these conditions can the right decision be made, and the physician will do well to avoid the two pitfalls; either to neglect the early symptoms where serious organic disease demands prompt and radical treatment, or, by misapprehending the significance of some of these signs of disordered menstruation, to undertake sterilizing and mutilating operations needlessly. We shall consider some of these problems in a logical order and begin first with the adolescent.

How do you manage, Dr. Low, the problem of the amenorrhoea of adolescence?

DR. LOW: The general attitude one should take in attempting to handle this problem should be that as a rule no active treatment is necessary before the age of 16-18 years. Close attention should be paid to the general health and environment of these young girls, and a complete physical examination is necessary and basal metabolism estimation is often helpful as indicating hypothyroidism. In many cases, the overly anxious mother requires considerable reassurance.

DR. COSBIE: I should like to add that the endocrine treatment of amenorrhoea is in the main disappointing in its results, and that usually in the absence of some definite organic disturbance, reassurance and general measures are all that are required.

In the excessive menstruation of the teen-

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age girl, what are the usual conditions found, Dr. Armstrong?

Dr. Armstrong: Many girls exhibit excessive menstruation as well as irregularity for periods of from several months to a year or more after the initiation of the function, and the most of these without treatment eventually fall into a normal rhythm and amount. In most cases this type of bleeding is anovulatory. Here again I should like to emphasize the importance of attention to the general health, diet and habits, and exercise of patients.

Dr. Cosbie: One should, of course, emphasize again the importance of the elimination of organic disease, but recognize that in this age group it is rare.

Dr. Noonan, is malignancy a possibility at puberty or before?

Dr. Noonan: Extremely rare, but but nevertheless, the possibility must never be forgotten. I recently saw in Rochester a child age 3, alive and well, who had to undergo a panhysterectomy at the age of six months for carcinoma of the cervix. The earliest report of malignancy that I have in mind was carcinoma of the ovary at between 6 and 7 months intra-uterine life.

Dr. Cosbie: And a grapelike sarcoma of the cervix, also very rare, can occur in infancy.

What would you say, Dr. Van Wyck, is the frequency of the granulosa cell tumour in childhood?

Dr. Van Wyck: The granulosa cell tumour, or more properly called granulosa cell carcinoma of the ovary, may occur at any age; although rare before puberty, its presence should be suspected whenever precocious menstruation is present, especially if there is a premature appearance of the secondary sex characteristics. The variability of the malignancy of these tumours makes the diagnosis of great importance.

Dr. Cosbie: *What are the possibilities when menstruation is precocious, Dr. Low?*

Dr. Low: I suppose one would define precocious menstruation as one where onset in this country at least is before the age of 10. In such cases one would naturally think of the occurrence of some follicle stimulating tumor of the ovary, such as granulosa cell tumor. Of course, there are types in which no endocrine gland lesion is demonstrable. Rare cases are due to adreno-cortical syndromes and perhaps the largest group of precocious puberty cases are constitutional in type, in which the puberty mechanism is set in motion unusually early and yet is otherwise normal.

Dr. Cosbie: In this latter group one might place the transient vaginal bleeding sometimes seen a few days after birth.

FUNCTIONAL UTERINE HAEMORRHAGE (BEFORE AGE OF 40)

What are the important diagnostic procedures in the treatment of functional uterine haemorrhage during the reproductive period in patients under 40?

Dr. Armstrong: The first and most important procedure in dealing with this problem is to exclude organic disease; in other words, to make sure that the bleeding is really functional and that no pelvic tumor is present. This can be done only by a thorough pelvic examination and a diagnostic curettage. And in these cases with excessive or irregular bleeding, the

classical curettage and biopsy is to be preferred to the less accurate examination of the exfoliated cells of the so-called vaginal smear. *Would you agree with that estimate of the value of the vaginal smear examination?*

DR. COSBIE: Yes, I believe that where there are the classical indications for curettage and biopsy, this should always be done, but should be done, of course, thoroughly, and include biopsy of any suspicious lesion of the cervix. The role of the smear is perhaps greater as a screening procedure and possibly also as a method of estimating the effect of radiation on the treatment of malignant disease; but I quite agree with you, Dr. Armstrong, that the diagnosis of functional haemorrhage in the present state of our knowledge is one of inference after the exclusion of all organic disease in the pelvis or elsewhere.

In such patients has curettage any therapeutic value, Dr. Noonan?

DR. NOONAN: Yes; in no other way than by curettage can malignancy be excluded, and also one has an opportunity to see the actual pattern of the endometrium. Frequently the curettage may be followed by a remission of the menorrhagia for at least some months, and one might hope that either the anovulatory function changes over to ovulation, or that an improvement in the patient's health may occur as the result of commonsense measures, or that the patient may become pregnant.

DR. VAN WYCK: That will cure the patient for at least nine months, or longer if the baby is breast-fed.

DR. COSBIE: Your suggestion, Dr. Van Wyck, might well be considered by the patient. Unfortunately, it is not always practicable. *What is your belief in the value of organotherapy in these patients?*

DR. VAN WYCK: It is in these patients where it is essential to preserve the reproductive function as well as the ovarian endocrine function that organotherapy, perhaps better known as endocrine therapy, has its greatest field. I have tried many types of such therapy and find it unpredictable, uncertain, and expensive. I am somewhat sceptical also of attributing the ultimate recovery of many of these cases to the endocrine therapy. I believe it is often rather due to an improvement in the general health of the patient, to correction of her diet and habits, or perhaps just to the natural tendency to a spontaneous reversion to a normal function.

DR. COSBIE: Dr. Low, is such endocrine therapy, and I assume that we are keeping in mind the usual types such as the use of stilboestrol, A.P.L., testosterone propionate—*is such therapy purely empiric, or can it be regarded as specific or controllable by laboratory findings?*

DR. LOW: In most cases organotherapy is empiric but diagnostic curettage to reveal the pattern of endometrium is of value as indicative of ovulatory or anovulatory bleeding.

DR. COSBIE: *Do you believe that the new work which concerns the glycogen content of the endometrium indicates the value of stilboestrol in these cases?*

DR. LOW: That work is of great interest but I do not believe as yet substantiates therapy.

DR. COSBIE: *What is the place of radiation in these cases?*

DR. ARMSTRONG: I do not believe there is much scope for radiation in a patient under 40 suffering from functional haemorrhage. Both radiologists and

gynaecologists are in agreement that radiation should be avoided in patients of this group even though the dose is merely minimal and designed only as a temporary arrest of menstrual function. I should prefer not to use it.

DR. COSBIE: *You would prefer repeated curettages?*

DR. ARMSTRONG: Yes, because there is no certainty as to the effect of even small doses of radiation on the future function of the patient or on a future pregnancy.

DR. COSBIE: *Well, then, Dr. Noonan, if we do not advise radiation in these cases for patients under 40, do you advise hysterectomy for functional haemorrhage?*

DR. NOONAN: I should prefer it to castration doses of radiation because the patient is too young for the very disturbing artificial menopause that seems to follow. I would hope, however, that after curettage, a trial of endocrine therapy, and patience, hysterectomy would rarely be necessary, and surely one need not regard such a radical step as necessary if, with or without palliative treatment, the patient's general health is not seriously disturbed. When, however, necessary, a hysterectomy permits not only a complete review of the pelvic organs but allows one to leave healthy ovarian tissue and so avoid an artificial menopause.

DR. COSBIE: *When a hysterectomy is indicated should it be total or sub-total?*

DR. VAN WYCK: It should be total in all cases where, when the removal of the body is necessary, the cervix can be removed without subjecting the patient to an undue added risk.

DR. COSBIE: I agree that the cervix should never be left behind when a hysterectomy is performed except in the very few cases, such as some cases of endometriosis for example, where the denseness of the adhesions in the lower part of the pelvis make the dissection of the cervix unduly dangerous. One must not forget, however, that 4% of the cases treated at the Toronto Institute of Radio Therapy occur in the stump of the cervix that has been left behind. Without being too radical, I believe that between 80 and 90% of all hysterectomies should be total.

When a hysterectomy is performed during the reproductive period do you remove both ovaries, Dr. Low?

DR. LOW: If the patient is under 40 years of age, every effort should be made to leave *in situ* at least one healthy ovary. Over 40 years of age I do not think it is important to leave an ovary or ovaries as ovarian function is as a rule decreasing and most symptoms of artificial menopause at this age are either very slight or easily controlled by minimal dosage of oestrogenic substance.

DR. COSBIE: The justification, of course, for being so radical after the age of 40 is the potentiality of carcinoma of the ovary.

DR. VAN WYCK: I should think it illogical at operation to leave an ovary which has ceased or is ceasing function at the menopause.

FUNCTIONAL UTERINE HAEMORRHAGE AT MENOPAUSE

DR. COSBIE: *In functional haemorrhage at the menopause what is the most important diagnostic consideration?*

DR. ARMSTRONG: Well, I believe we have already said this, but it is always worth saying again and again, that the most important diagnostic con-

sideration is a thorough pelvic examination including a curettage and biopsy of both the cervix and the body of the uterus, and one must not forget that it is at this age, that is at or during the menopause, (to be definite between 40 and 50 years of age,) that functional haemorrhage is in competition with serious organic disease. Whereas one may occasionally assume a functional diagnosis at puberty without a curettage, to omit this important diagnostic procedure at the menopause is a serious dereliction of duty.

DR. COSBIE: *Would you use organotherapy, Dr. Noonan, in this age group for functional bleeding?*

DR. NOONAN: After the period of childbearing is over, I have no hesitation where palliative measures fail, and where the blood loss is interfering with the patient's general health, in advising radical treatment either by castration radiation, which will abolish completely ovarian function, or perhaps preferably by hysterectomy. Organotherapy can be tried, of course, where one is confident that cancer does not exist, but, when prompt relief is needed, I should prefer radiation or hysterectomy.

DR. COSBIE: *How would you describe the place of radiation in these cases, Dr. Van Wyck?*

DR. VAN WYCK: I agree with what Dr. Noonan has said about radium therapy in these cases. There is no doubt that 100% of these patients properly selected can be cured by castration radiation, that is the intra-cavitary insertion of 1600 to 1800 milligram hours of radium properly screened. I believe, however, that unless the uterus is small, moveable, and it and the rest of the pelvis proven to be free of neoplasm, a hysterectomy is preferable when such radical treatment is necessary.

DR. COSBIE: I am in agreement with that because one cannot help but keep in mind the possibility of a cancer which has been missed by the curette or the taking of a biopsy, or the possibility of an as yet unsuspected ovarian malignancy.

DR. VAN WYCK: I also believe another contra-indication to radium therapy is the presence of a retroversion with marked retroflexion, or the presence of pelvic pain.

DR. COSBIE: In other words, when you advise radium, you select your cases most carefully. *Dr. Low, what do you feel are the limitations of or contra-indications for radium therapy in these cases?*

DR. LOW: I think the contra-indications for radiotherapy here are those patients in whom lower abdominal pain is a predominant symptom. I also often hesitate to use radiotherapy where the uterus is markedly retroverted or retroflexed, or where there is considerable prolapse of the uterus and pelvic floor.

DR. COSBIE: And, of course, when you speak of radiotherapy you are thinking entirely of radium and not X-ray therapy.

DR. LOW: Well, the effect of either is, of course, similar and in properly selected cases will achieve a cure. I prefer radium rather than X-ray when I wish this type of therapy, perhaps largely because it enables me to do the essential preliminary diagnostic curettage, and should I encounter unsuspected carcinoma of the body of the uterus, I will then give an adequate dosage for the cure of the cancer. However, I prefer hysterec-

tomy at or after the menopause rather than radiation except in a few carefully selected favourable cases.

DR. COSBIE: Well, I think we all agree on that and it is possible that the tendency to swing away from radiation in these cases to hysterectomy has been fostered by the decreasing danger of the operation.

DR. COSBIE: *What special precautions should be advised when intra-uterine radium is used, Dr. Armstrong?*

DR. ARMSTRONG: Well, I should list them as meticulous surgical technique, the use of alcohol as a local antiseptic, and the careful dilatation of the canal. One must know the direction of the axis of the uterus, must avoid overdilatation which could result in the rupture of a small uterus, the careful placing of the radium properly screened, and sufficient packing to prevent the radium slipping out of the uterus.

DR. COSBIE: *Is the ovary a usefully functioning organ after the menopause?*

DR. NOONAN: I do not believe it has much physiological use after the menopause. I agree with what Dr. Low advised in the removal of ovaries both during and after the menopause.

BLEEDING DURING THE PUERPERIUM

DR. COSBIE: *What may be the cause of irregular bleeding during the months following childbirth?*

DR. LOW: It may be quite usual for the first menstrual flow after childbirth to be somewhat irregular. If the irregularity continues or the flow becomes profuse one should think of placental remains, subinvolution of the uterus, unrecognized fibroid tumors or polyp and finally, the possible development of choriocarcinoma.

DR. COSBIE: Here, again, when in doubt a curettage would be useful and, of course, with a previous history of hydatid mole the A Z test (positive in dilution) would suggest choriocarcinoma.

How do retained secundines affect the puerperal patient?

DR. ARMSTRONG: Haemorrhage, sepsis, subinvolution are obvious results, and one might go on to add retroversion, weakening of the pelvic floor with the remote effects on the menstrual and reproductive function.

DR. COSBIE: In other words, Dr. Armstrong, you do not treat retained secundines casually, and I feel that you are right. Meticulous attention to the expulsion of the placenta and membranes is a primary function of the obstetrician.

How would you define subinvolution of the uterus, Dr. Noonan?

DR. NOONAN: Clinically by palpable evidence that the return of the uterus to its normal size was slower than usual. When this occurs one is not surprised to find this condition associated in the puerperium with prolonged bleeding, sepsis of some degree, and a slow general convalescence.

DR. COSBIE: In just such cases, of course, one must be careful to detect neoplasms, either benign or malignant, in the uterus.

When amenorrhoea is prolonged in the puerperium, should one suspect a new pregnancy?

DR. LOW: One should always suspect pregnancy when amenorrhoea is present in a woman during the reproductive age, but it is not uncommon to see late onset of menstruation following childbirth. In fact, occasionally one will encounter the so-called hyperinvolution of the uterus as a result of

which the patient may never menstruate again.

FIBROIDS

DR. COSBIE: *How common are fibroids during the reproductive period?*

DR. VAN WYCK: Perhaps 20% of all women over 35 years of age harbour these growths.

DR. COSBIE: *Does one ever see them before puberty?*

DR. LOW: I have never seen fibroids of the uterus prior to puberty.

DR. COSBIE: *Do fibroids cause trouble after the menopause?*

DR. ARMSTRONG: As fibroids usually disappear after the menopause their persistence suggests some type of degeneration, possibly malignant.

DR. COSBIE: *What is the relation of sterility to fibroids?*

DR. NOONAN: Fibroids may cause sterility by distortion or occlusion of the cervical canal, but even when these do not occur, it is possible that fibroids may produce exudates from the uterus which are hostile to the passage of the spermatazoon.

DR. COSBIE: *Under what circumstances should one operate on fibroids?*

DR. VAN WYCK: Many fibroids do not need operative removal. Only if they produce menorrhagia, pain, or other disturbance of function from their rapid growth, need the fibroids be removed.

DR. COSBIE: *Would you operate on fibroids during pregnancy?*

DR. LOW: It is seldom necessary to operate for fibroids complicating pregnancy. Acute degeneration of fibroids which does not subside but gives increasingly serious symptoms of acute pain and signs of peritonitis may call for operative interference.

DR. COSBIE: *When you decide to operate for fibroids, Dr. Armstrong, how do you decide between myomectomy and hysterectomy.*

DR. ARMSTRONG: I believe a myomectomy should be done whenever the reproductive function may thus be preserved. There is perhaps an increased risk of embolism following myomectomy. This risk must be balanced by the desirability of further pregnancy.

DR. COSBIE: A very important point. This rule applies even if there are many fibroids.

DYSMENORRHOEA

What are the clinical problems of dysmenorrhoea?

DR. NOONAN: Primary dysmenorrhoea is menstrual pain in the absence of any significant pelvic lesion. It could also be called essential, functional, or idiopathic. It can only be diagnosed, of course, by excluding the secondary causes where there is some demonstrable pelvic disease.

DR. COSBIE: *In these essential cases, what are the results of endocrine treatment?*

DR. VAN WYCK: The problem is usually a combination of constitutional, psychogenic and endocrine factors, and I believe that the management of these cases depends more on the two former than on the latter. On the whole I have had disappointing results from endocrine therapy in dysmenorrhoea, and I am afraid I try to help these patients more with reassurance, control of their habits, and while doing so, attempt to tide them over the worst of their pain with codeine and aspirin.

DR. COSBIE: *You believe in the psychosomatic approach. Do you value this principle, Dr. Low?*

DR. LOW: I think this is one place where a psychosomatic approach is of very definite value. Once organic pelvic disease has been ruled out, I feel there are very few cases of so-called essential dysmenorrhoea that require active surgical treatment.

DR. COSBIE: *When would you advise dilation of the cervix?*

DR. ARMSTRONG: In the very severe intractible cases I might consider a dilatation of the cervix, and even in a few cases a pre-sacral neurectomy. The dilatation may give relief permanently; if not, sometimes a second dilatation is more effective.

DR. COSBIE: *What is your opinion of the value of dilatation of the cervix in essential dysmenorrhoea, Dr. Noonan?*

DR. NOONAN: I would try it where other treatment fails but often the results are disappointing. I believe that if a stem pessary has been used, dilatation will probably give the patient about two months relative comfort, and give a little more time while one might be considering a pre-sacral sympathectomy.

DR. COSBIE: In the past I have used the stem pessary, but one must not forget that the presence of a foreign body in the cavity of the uterus for a prolonged period, may be the cause of pelvic inflammation. *What is your opinion of the role of pre-sacral neurectomy in these cases?*

DR. VAN WYCK: This operation is a rational and effective procedure in the occasional unusually severe case which has been reported and, of course, it could be performed as a supplementary procedure in secondary dysmenorrhoea in conservative operations for endometriosis.

DR. COSBIE: I agree with the conservative approach to the problem of dysmenorrhoea. Too many ill-judged operations are done for this symptom and this calls to mind another class of cases where the discovery of a small, cystic ovary in various menstrual disorders has led to needless laparotomies. *What is your opinion, Dr. Low, about these women who have been obviously subjected to an ovarian operation on insufficient grounds and with no improvement?*

DR. LOW: There has been no operation so abused as the one where the patient states, "I had my appendix removed and one ovary or a cyst on one ovary." This is mainly because the surgeon does not recognize normal ovarian physiological changes.

DR. COSBIE: This discussion has covered a wide field, but I believe it has brought out a great many of the important practical considerations which should be the concern of the practitioner. I should like to point out the strong emphasis that one always finds to-day among a group of gynaecologists—emphasis upon a conservative approach to these problems with a view to the preservation of the reproductive and sex function. Progress during the past decades has been made in many ways in the treatment of these disorders. This could be summarized under three headings:

1. A better understanding of the normal physiological factors involved;
2. A technical improvement which renders operative procedures much safer; and most important of all,
3. A realization of the major duty of the gynaecologist which is impressed upon him because he is also an obstetrician; and so he appreciates the means and the value of the preservation of the reproductive function.

IDIOPATHIC EPILEPSY

DAVID I. GOVE, 5T0

DEFINITIONS

EPILEPSY MEANS SEIZURE and, like angina pectoris, is a symptom and not a disease.

Toward the end of the 19th century Hughlings Jackson defined epilepsy as "occasional, sudden, excessive, rapid and local discharge of gray matter." This is a truly remarkable definition when one considers that Berger did not produce his first electro-encephalograms until 1929. Jackson's definition presents a clear and concise picture of the seizure in spite of minor objections to its terms. A more modern but distinctly less euphonious definition is "symptomatic, paroxysmal, cerebral dysrhythmia."

INCIDENCE

General Population

Figures for the incidence of epilepsy in the literature deal, in most cases, with both idiopathic and acquired forms of the disease. In a series of 2000 patients, however, Lennox has shown that in 77% the cause of seizures could not be demonstrated.

The most frequently quoted figure for the incidence of epilepsy in the general population is that of 0.5% amongst draftees for the U.S. army in the first world war. This represents the incidence amongst a selected group and could probably be revised upward to give a more accurate picture.

Sex

According to Lennox and Cobb, patients are 58% male. The greater incidence in males has been explained as a result of greater trauma to the male head during and after birth.

AETIOLOGY

General Factors

HEREDITY. Lennox has made an excellent study of the hereditary factor in epilepsy. He finds that the incidence of seizures amongst blood relatives of both idiopathic and acquired epileptic patients is 2.7%. The hereditary influence as determined in this manner is 8 times greater in migraine than in epilepsy, 2 times greater in obesity and approximately the same in diabetes and epilepsy. Dividing his cases into idiopathic and acquired groups, he finds the seizure incidence to be 3.0% amongst relatives of the former and 1.4% amongst relatives of the latter. His conclusion is that the greater the genetic factor, the less the acquired factor necessary to produce seizures.

Lennox makes the general observation that predominantly hereditary affections tend to appear earlier in life than acquired conditions. His survey reveals that the greater the hereditary influence —as indicated by the number of blood relatives having seizures—the earlier in life the disability appears. Females show a greater hereditary factor than males, possibly accounting for the earlier appearance of convulsions in girls.

An extensive study of twins showed that amongst monozygotic twin pairs without evidence of brain pathology, both twins were epileptic in 94% of cases. Amongst monozygotic twins, one of whom showed evidence of brain path-

ology, both twins were epileptic in only 17% of cases.

FACTORS AFFECTING SEIZURE THRESHOLD. Three factors have been known for many years to decrease the seizure threshold in epileptics. These factors are hydration, alkalosis and reduced oxygen tension in the inspired air.

Water metabolism of epileptic patients between seizures is normal insofar as it is revealed by fluid intake and output, blood and plasma volume. McQuarrie has shown that sudden storage of water by epileptics produces grand mal seizures in 12-48 hours. Water storage was accomplished by simultaneous administration of pitressin and large amounts of water. When enough salt was fed to maintain extracellular osmotic pressure, no convulsions were induced. Creating a negative water balance resulted in a decreased number of seizures.

No abnormalities in acid-base balance have been demonstrated in epileptics during or between convulsions. Alkalosis induced by overventilation or ingestion of alkalis, however, has been shown to be a factor in the production of seizures in experimental situations. In vitro studies have shown that, within certain limits, the excitability of nervous tissue varies directly with its pH.

Acidosis produced by high carbon dioxide concentrations in the inspired air, acidifying salts, muscular exercise and a ketogenic diet reduces the number of seizures in epileptic patients.

Petit mal attacks tend to be increased when the oxygen tension of the inspired air is low and reduced when it is high. Investigations, however, have demonstrated that oxygen consumption before, during and after fits is normal in epileptics. The oxygen tensions of arterial blood and of venous blood from brachial and internal jugular veins is not significantly different in epileptics and in control groups of non-epileptics.

METABOLISM IN EPILEPTICS. Studies of protein and carbohydrate metabolism in epileptics reveal no significant abnormalities. Levels of blood lipoids reveal distinct but as yet unexplained variations from normal. Blood cholesterol values are normal or low between convulsions. During a convulsion there is a fall in cholesterol with a redistribution such that more appears in cells and less in serum. The cholesterol to lecithin ratio of the blood is highest at or near a convulsion and lowest at a time most remote from a convulsion.

Even more interesting changes in mineral metabolism are associated with convulsions. Between seizures body fluid levels of calcium, phosphorus, potassium and magnesium are normal. During a convulsion, increases in serum levels of calcium, phosphorus and potassium have been demonstrated, together with a decrease in serum magnesium. Most of these changes are probably secondary to the convulsion but the interesting observation has been made that a rise in serum and urinary potassium antedates an attack by 36 hours.

CEREBRAL FACTORS

CEREBRAL CIRCULATION IN EPILEPTICS. For many years a theory of the cause of seizures was that of a sudden local or generalized cerebral vasoconstriction. This theory appears to have been based on the observations of neurosurgeons made at operation. Penfield, however, has published a large series of observations which contradict the cerebral anaemia theory. He describes no pre-seizure pallour or vasoconstriction in the cortex. The first sign of a seizure is cessation of pulsation in pial vessels. This is interpreted as evidence of vasodilatation.

Hyperaemia is apparent in a local epileptogenic focus during and following a seizure. Penfield believes these vasomotor phenomena are a result of increased carbon dioxide production by discharging nerve cells.

NERVE CELL PERMEABILITY AND SEIZURES. Following his demonstration of hydration as an experimental means of producing seizures in suitable subjects, McQuarrie postulated a disturbance in the surface functions of the nerve cell membrane as the characteristic defect in epilepsy. This has led to numerous investigations of cellular permeability and electrolyte changes in the epileptic cortex. Spiegel, Spiegel-Adolf and Henny demonstrated that cortical permeability is increased by conditions producing a lowered convulsive threshold or actual convulsions, namely, alkalosis, hydration, hyperventilation, increased intra-cranial pressure, electrical stimulation of the brain and convulsant drugs.

A recent analytical study of the electrolytes of the epileptic cortex by Colfer revealed a consistent redistribution of electrolyte in cerebral cortical neurones resulting in their loss of potassium and gain in sodium. Similar changes were obtained in vitro by increasing the pH of the cortex.

ORIGIN AND SPREAD OF THE EPILEPTIC DISCHARGE. The site of the epileptic discharge has been more closely investigated from the standpoint of acquired epilepsy. Penfield cites two general rules with regard to the origin and spread of the discharge which seem equally applicable to idiopathic and acquired forms. Discharges spread by normal neuronal pathways and not from one group of nerve cells to another in close proximity to it. No matter what the site of the original discharge, spread is always by direct routes toward the sensorimotor cortex. In abortive attacks, the discharge may cease before reaching the Rolandic fissure and in this way seizures can be produced without the motor signs commonly associated with epilepsy.

Recent work by Jasper and Droogleever-Fortuyn seems to point unmistakably to the diencephalon as the source of discharge in petit mal.

Common Precipitating Factors in Epileptic Seizures

Many factors have been described as precipitating epileptic seizures. The onset of a menstrual period and constipation are thought to act by increasing fluid retention by the tissues. Alcoholism is a well-known cause of cerebral oedema. Fatigue precipitates seizures in many patients but the mechanism is unknown. Psychological factors will be discussed later. In most cases, however, no specific precipitating factor can be discovered.

CLINICAL MANIFESTATIONS

Symptomatology

Kinnier Wilson discusses the symptomatology of the disease under the following four headings:

PRODROMES. Prodromal symptoms are to be distinguished from auras. Prodromes precede seizures by months or days; auras immediately precede and merge with a seizure. Prodromes may be motor or sensory in type. The commonest motor prodrome is the myoclonic twitch—a sudden start affecting one or other limb. Restlessness, yawning or sneezing are less common.

Sensory prodromes comprise headache, vertigo, paraesthesiae and various psychic changes such as irritability, apathy and depression. At times feelings of extreme physical and mental well being precede seizures.

AURAS. Penfield regards auras as

sensory seizures which have value in localizing the site of the epileptogenic focus. This appears to be true of only a limited number of auras. Auras occur in 50-60% of patients subject to seizures.

Somatic sensory auras consist of numbness, tingling or pins and needles sensations. They are frequently localized to small areas at first and are then felt to ascend toward the head whereupon consciousness is lost.

The commonest aura is classed as visceral sensory and consists of an epigastric sensation variously and vaguely described by patients. Complex or psychical auras consist chiefly of dreamy states shown by Jackson to be associated with lesions of the temporal lobe.

Special sense auras are chiefly visual or auditory. Visual auras range in complexity from simple sensations of light to hallucinations in which objects, faces and figures may appear. Auditory auras vary from simple hissings and buzzings to repeated phrases, singing and instrumental music. Gustatory and olfactory auras also occur.

CONTENT OF THE FIT. The two chief forms of seizure are the major and the minor fit. In a grand mal convulsion, the patient falls to the ground and his musculature is seized by a powerful tonic spasm. The upper limbs are flexed and adducted, the lower limbs extended with inversion and plantar flexion of the feet. Apnoea occurs and is followed by cyanosis. Slight muscular vibrations follow and become abrupt, forceful jerks. Stertorous breathing occurs and frothy saliva wreathes the lips. Incontinence of urine or faeces may occur. With a last jerk the clonic stage ceases and the patient lies lax. A stage of deep slumber of variable length intervenes before consciousness returns.

Serial epilepsy denotes a succession of grand mal attacks at brief periods over a short interval. Status epilepticus means a series of grand mal attacks between which the patient does not regain consciousness. As many as 500 convulsions have been recorded in 24 hours. Death may follow the onset of coma. Status is uninfluenced by age, sex or age of onset of epilepsy.

Symptoms of petit mal seizures may be hard to detect. The patient may lose consciousness or suffer from brief mental confusion. A vacant stare, suspension of activity, rolling up of the eyes may be the only objective signs of an attack. The return to full awareness is sudden and activity may be resumed without a falter.

SEQUELAE. Physical and psychical sequelae of convulsions are described. Headache, vomiting and myalgia may follow an attack. Transitory hemiplegias are not unusual after severe attacks. Accidents due to the violence of the convulsions are frequently seen.

Temporary psychical disturbances often follow the seizure. Post-epileptic automatisms vary widely in extent and duration from a brief fumbling in the pockets to long walks covering amazing distances. Nocturnal seizures are frequently responsible for somnambulism.

Clinical Variants

Numerous clinical variants of the epileptic seizure occur. They are classified as motor, sensory, psychical and visceral forms.

The most interesting motor variant is the Jacksonian or local seizure. It is a rare symptom of idiopathic epilepsy. Myoclonic twitches may be the sole sign of the disease. Tonic fits resembling decerebrate rigidity proceed chiefly from structural disease. Co-ordinate seizures are those in which purposive actions

are performed. Amnesia is present and when unconsciousness does not supervene, the condition is termed psychomotor epilepsy.

Pyknolepsy is a variant of petit mal consisting of endless repetitions of the minor fit. The disease is of abrupt onset and tends to disappear spontaneously and completely.

The chief sensory variants are the sensory march, reflex epilepsy and affective epilepsy. The sensory march is a sensory fit closely resembling the motor march which may be seen in cases of Jacksonian epilepsy. Reflex epilepsy is a term applied to convulsions immediately precipitated by external stimuli. Affective epilepsy signifies a fit induced by disturbing emotional factors.

Some authors consider the outbursts of anger and erratic conduct seen in some epileptics to be psychical equivalents of the epileptic seizure. This concept has not received general support.

Visceral variants may accompany grand mal or petit mal seizures in the form of loss of sphincter control.

The Epileptic Temperament

There are two aspects of the psychological problem of epilepsy. The first is the concept of the epileptic personality and the second, the importance of psychic factors in the precipitation of seizures.

A review of the literature reveals a rather marked cleavage of opinion on these matters. To make a generalization, neurologists tend to minimize both aspects while psychiatrists lean in the opposite direction and this is especially true of psychiatrists whose experience has been largely with institutionalized patients.

In recent years there seems to have been a tendency to discredit the theory that there is an epileptic personality which is an integral part of the disease and which may be commonly discerned even before the appearance of convulsions. It is more common at present to regard the abnormal personalities of some epileptics as results of the social implications of seizures.

There seems little doubt that emotional factors are important in the precipitation of fits. It is considered unlikely, however, that this can be accepted as a major cause of epilepsy.

DIAGNOSIS

The diagnosis of idiopathic epilepsy depends on clinical and laboratory findings common to other neurological disorders. While epilepsy as a symptom may be diagnosed simply by a history obtained from someone who has witnessed the seizure, the diagnosis of idiopathic epilepsy as a disease in many cases requires a far more complicated investigation.

A detailed history is necessary with an account of seizures in blood relatives of the patient in addition to a careful description of the seizure pattern obtained from a reliable witness. In almost all instances, the patient's account of his own attack is quite useless for diagnostic purposes. Past history of head injuries and neurological disease should be obtained. A complete physical examination with particular attention paid to neurological features and ophthalmoscopic examination should be carried out. If the patient is hospitalized, a hydration regimen may be advisable so that an exact description of the seizure can be obtained.

Laboratory investigations should include an examination of cerebrospinal fluid. Any marked deviation of C.S.F.

contents or pressure from normal makes a diagnosis of idiopathic epilepsy very hazardous. X-ray studies of the epileptic patient should include encephalography and ventriculography. Minor x-ray signs of cerebral pathology can be interpreted only by an expert neuroradiologist.

Electroencephalography is a valuable diagnostic procedure in epilepsy but its limitations must be remembered. In the absence of adequate clinical, laboratory and x-ray studies, its usefulness is slight. In a paper of this length it is impossible to deal with the complicated interpretation of electroencephalographic studies but it is felt wise to mention the fact that non-epileptics may give abnormal recordings while a few epileptics show normal tracings.

In the investigation of the epileptic patient, it would be wise to keep in mind a classification of the epilepsies. The following is an aetiological classification suggested by Penfield and Erickson:

1. With Demonstrable Cerebral Lesions:
   - *a.* expanding lesion:
     Neoplasm, chronic abscess, etc.
   - *b.* cerebral cicatrix:
     Trauma, infection.
   - *c.* local cerebral atrophy:
     Compressions, ischaemias, infections.
   - *d.* local microgyria:
     Infantile compression or ischaemia.
   - *e.* brain cyst:
     Vessel closure or haemorrhage.
   - *f.* diffuse cerebral disease:
     Degenerations, infections, sclerosis.
   - *g.* diffuse cerebral vascular disease:
     Arteriosclerosis, syphilis, etc.
   - *h.* miscellaneous:
     Congenital lesions, etc.
2. Without Demonstrable Cerebral Lesions:
   - *a.* idiopathic.
   - *b.* toxic and febrile.
   - *c.* hypoglycaemic.
   - *d.* miscellaneous.

The diagnosis of idiopathic epilepsy in a patient whose seizures began after the age of 20 must be made only after a complete examination in all the fields mentioned and neurological consultation is probably indicated.

PROGNOSIS

In the past 30 years the advances made in the symptomatic treatment of epilepsy have been cause for optimism in prognosis. In the absence of gross pathology and mental deterioration, the patient's chances of overcoming the barriers to a normal life are, in general, good. Spontaneous remissions are not thought to occur in more than 10% of patients but are more likely to occur in cases of idiopathic than in cases of acquired epilepsy. The greater the number and frequency of attacks, the worse the prognosis for spontaneous remission. As is the case in most diseases, a number of epileptics are refractory to all forms of symptomatic treatment.

TREATMENT

The Individual Attack

While a single convulsion is seldom fatal, it is necessary to protect the patient from injuries to which the violence of his convulsive movements may expose him. A soft gag should be placed between the teeth to protect the tongue. Occasionally respiration may be em-

barrassed by aspirated food or vomitus and an airway will have to be established.

Status epilepticus must be treated energetically since it may prove fatal. In most cases it is precipated by sudden cessation of medication. Sodium phenobarbitone may be given intramuscularly or paraldehyde by rectum. In stubborn cases ether anaesthesia to surgical levels may be used. Magnesium sulphate as a retention enema or intravenously may be given to reduce cerebral oedema. Adequate nursing care, including catheterization where necessary, is essential.

Continuing Treatment

DRUGS. Bromides were the first drugs used successfully in the treatment of epilepsy and are still recommended in cases in which tolerance to other drugs develops. They are more effective when combined with a reduced chloride intake but toxic effects must be watched for. It is usual to start with a dose of 2-3 Gm. daily and increase or decrease as indicated. Bromides may be combined with phenobarbitone.

Of the barbiturates, phenobarbitone is the most effective. Dosage should be arranged so that the maximum amount is taken just before the time at which seizures occur. For this reason a schedule must be fitted to each individual patient. Total daily dosage may range from 60-600 mg. depending on the frequency of seizures. Benzedrine sulphate is occasionally necessary to combat the drowsiness caused by large doses.

These two drugs are almost equally effective in cases of grand mal and petit mal. Recently, drugs have been introduced which are more specific in their usefulness. Sodium diphenyl hydantoinate is useful in grand mal and psychomotor seizures. It is customarily given in doses of 100 mg. three times a day at first with a later adjustment of dosage to a satisfactory level. Toxic effects are gingival hyperplasia and exfoliative dermatitis. Fatalities have been reported from its use. Mesantoin, a more recent drug of the same series, is reported to have fewer toxic effects.

Tridione appears to be fairly specifically effective against petit mal. The common dosage is 0.3 Gm. four times a day.

GENERAL MEASURES. Ketogenic diets have been used and found effective in the control of seizures especially in young patients. As with any dietary regimen, it is difficult to ensure that a proper routine is being followed. Schemes of dehydration have been suggested but are not particularly satisfactory.

Many factors in the patient's life must be adjusted if satisfactory control of seizures by means of drugs is to be achieved. An occupation free from hazards which might prove fatal during a seizure must be found. Driving an automobile, climbing ladders and scaffolding and work near industrial machines should be avoided. Complete abstinence from alcohol is important. Psychotherapy in an effort to overcome anxiety, fear and anger is indicated where these emotions are thought to be factors in the precipitation of seizures.

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THE POST-THROMBOTIC SYNDROME

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THE PATIENT with a chronically oedematous lower leg with skin lesions in the form of bronze coloured areas of induration and typical ulcers in the region of the medial malleolus plus a complaint of bursting pain and sensations of heaviness and tiredness in the affected limb presents a syndrome which has been known to the medical profession for centuries.

Some decades ago this condition was considered purely as a skin lesion, to be treated by the dermatologists. Later, varicosities of the subcutaneous veins were held responsible and for many years the familiar ulcers were termed "varicose ulcers."

Only in the past ten years has the aetiological role of thrombosis become apparent and the ulcers have now been termed "post-thrombotic" or "post-phlebitic" ulcers.

INCIDENCE

The work of Birger, Bauer and others now indicates that the commonest cause of the lower leg syndrome is previous venous thrombosis. In various series, it has been stated that from 40-87% of all crural ulcers are post-thrombotic.

Of those suffering acute venous thrombosis about 75% or more go on to have post-thrombotic sequelae in months or years. The condition is 2 to 5 times commoner in the female.

CLINICAL PICTURE

Post-phlebitic sequelae includes oedema, pain, induration of tissues, pigmentation, eczema, ulceration, recurrent episodes of acute thrombophelebitis, recurrent erysipeloid attacks and the formation of secondary superficial varicose veins. By far the commonest picture presented is that described in the opening paragraph of this presentation.

The usual sequence of events is as follows. Venous thrombosis occurs in one or both lower limbs following parturition, trauma, surgical operations, medical illness, fracture, etc. The acute phase with pain, swelling, increased temperature, tenderness over the involved venous trunks, positive Homan's sign and possibly pulmonary embolism subsides under treatment. In a matter of days or a few weeks the patient returns to normal activity. Often the patient is perfectly well, does not notice any swelling, and has no subjective complaints right up until the time that oedema, eczema, induration and ulceration arise fairly acutely. This may occur in a year of within 2, 5, 10 years or even 30 years after the acute phase. Usually, however, some oedema persists from the onset of thrombosis. Pain of a dull, bursting type may also be an early indication that all is not well.

The chronically oedematous limb favours the occurrence of streptococcal infection and a few patients suffer from recurrent erysipeloid attacks. Chills and fever are associated with burning, itching, pain and redness in a swollen extremity.

PATHOLOGIC-PHYSIOLOGY

Thrombosis, in 90% of instances, arises in the muscular veins of the foot and calf and proceeds proximally to involve the popliteal and femoral veins,

causing aseptic phlebitis and periphlebitis as it goes.

In the majority of instances the thrombus later becomes canalized and thus a rigid, tubular structure without valves is formed. Since there are no venous valves proximal to the junction of the long saphenous and femoral veins an uninterrupted column of blood extending from the heart to the lower part of the leg is formed. Thus, in the erect patient, gravity exerts its full force, there is retrograde flow in the abnormal venous channel and increased venous pressure in the lower part of the limb. A condition of "chronic venous insufficiency" occurs which serves to explain, partly or completely, all the post-thrombotic phenomena.

Œdema and Induration

Venous hypertension plus lymphatic obliteration, caused by the periphlebitis, accounts for a protein-rich oedema fluid which, by virtue of its irritant action, is said to be responsible for fibroplastic changes in the subcutaneous tissues—the characteristic induration.

Vasospasm is said by some to be the main cause of oedema. Afferent impulses arise in the involved segment of vein, efferent impulses pass to the vessels via sympathetic channels. The arteriolar constriction so produced abolishes arteriolar pulsation (a factor in propelling oedema fluid back into the circulation), and produces capillary anoxia with consequent increased capillary permeability. Constriction of venules increases hydrostatic pressure in the venous end of the capillary and so leads to further oedema production. That vasospasm is prominent in the acute stage of thrombosis is undisputed.

Ochsner and DeBakey consider that although not clinically evident it also plays an important part in the chronic second stage of thrombosis—the post-thrombotic syndrome.

Pain

This is attributed variously to chronic venous hypertension, to nerve irritation by perivascular fibrosis and to vasospasm.

Pigmentation

Venous hypertension results in capillary haemorrhage. Liberated haemoglobin becomes haemosiderin.

Secondary Superficial Varicosities

Retrograde flow in the deep veins necessitates dilatation of the superficial collaterals. They become widened and tortuous and their valves incompetent.

Ulceration, Eczema, Low-grade Infection

These are accounted for by "decreased tissue vitality" as the result of venous stasis with oedema and induration.

Ulceration occurs after the slightest trauma or may follow eczema, or arise spontaneously.

Low grade infection, including fungous infections is common.

That chronic venous insufficiency is chiefly responsible is corroborated by the fact that all but the very extensive ulcers will heal following bed rest with elevation of the limb—a state where retrograde flow is reversed and venous pressure is reduced to almost nil.

TREATMENT

1. Conservative: bland ointments, compression bandaging

e.g. Unna's Paste Boot.

The leg is painted up to the knee with Unna's paste, a gauze or elastic bandage applied, more paste, another bandage, etc., the whole being covered by a flannel bandage. The first boot remains

for a week, the second for two weeks, the third for three weeks. At the end of this six week period the ulcer is usually healed and the patient has remained ambulatory. A fourth boot may have to be applied. The patient is then instructed to bandage her own leg with an elastic bandage, removing it only at night for a much needed airing.

A simple elastic bandage may suffice without the use of pastes or ointments. It is important that the heel be covered.

This therapy produces good immediate results but almost inevitably there is recurrence in months or a few years. The same is true of bed rest and elevation of the limb.

2. Surgical

a. SUPERFICIAL FEMORAL VEIN INTERRUPTION with or without ligation of secondary superficial varicosities. The rationale of superficial femoral vein ligation depends on the fact that "chronic venous insufficiency" is the cause of the post-thrombotic lesions. For the same reason many advocate the ligation of superficial varicosities at the site of entry of communicating veins which are also ligated. Linton and Hardy are so impressed with the role of the latter that they combine superficial femoral vein interruption with ligation and stripping of the long and short saphenous veins.

Superficial femoral vein interruption has given encouraging early results. Reports on late results are awaited.

b. POPLITEAL VEIN LIGATION AND EXCISION. Bauer has demonstrated venographically and at operation that in cases where recanalization of thrombus in the femoral vein does not occur, satellite veins are formed in the adventitia and perivascular tissues of the occluded vein which conduct blood in a retrograde manner past the occlusion to the popliteal vein. He advocates popliteal interruption, particularly since communicating veins may empty into these vessels, thus adding a further blood volume to the retrograde stream. In Bauer's hands this has produced spectacular immediate results with relief of pain, oedema, and ulceration. Late results are awaited.

c. SYMPATHECTOMY. Ochsner and De Bakey test for vasospasm by doing lumbar sympathetic procaine blocks. In its presence and when its lasting relief is desired, they advise sympathectomy.

The operation is also advised to increase blood flow to the ulcer area and thus hasten healing, and to aid in the clearing-up of fungous infections by virtue of the anhydrosis it produces. It would appear to be an adjunct to other measures.

Local skin grafting and modified Kondoleon operations have been used extensively in the management of crural ulcers. Recurrences of ulceration are extremely common if these procedures are performed alone.

A combination of methods may prove advantageous in many cases. For example, the pre-operative healing of an infected ulcer using compression bandages will prevent the frequent post-operative complication of wound infection so common in these cases.

At the time of writing, deep vein interruption seems to offer most in the management of the severely involved post-thrombotic limb.

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THE COMMON COLD—RECENT INVESTIGATIONS

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A STATISTICIAN'S IDEAL, the common cold has wormed its way into the minds and throats of the human species to an extent beyond that of any other medical phenomenon. The infection, reduced by the medical dictionaries to merely "a catarrhal or other disorder of respiratory tract sometimes caused by exposure to cold and wet", was none-the-less chosen by radio's Orson Welles as the only effective earthly combatant of his men from Mars.

A great volume of sensational literature has been published on this subject. The literate layman is well enough aware that the common cold afflicts the average American from one to four times a year. He recognizes as true the fact that it represents an annual collective economic loss of $1,000,000,000 in America. He does not even tremble at the warning that although it is rarely the direct cause of death, it precedes or incites such serious infections as bacterial pneumonias, subacute bacterial endocarditis, septicaemia and meningitis, and often precipitates the symptoms of coronary occlusion, peptic ulcer and various other diseases (20).

This paper makes no attempt to describe completely either the nature of the common cold or the history of its investigation. It merely proposes to review, for those who would have an up-to-date conception of this important infection, the recent publications on the subject.

THE NATURE, THE AGENT AND THE CONTRACTION OF THE INFECTION

NATURE

The identification of the various types of infections of the upper respiratory tract is difficult, as complete bacteriological differentiation is not yet possible. Definition through establishment of clinical criteria is not simple, since objective signs and subjective symptoms are unreliable guides. Dingle (1) has identified two types of common cold as distinct entities; a coryzal type and a pharyngeal type, with incubation periods of 1-2 and 3-9 days respectively. Fox and Livingston (2) were unable to differentiate either spontaneous or induced colds on the basis of clinical characteristics or incubation periods. Differences in colds induced by the same agent were seen by these authors—symptoms of six subjects inoculated with an active agent varied from no colds in two cases to bronchopneumonia in another.

Attempts have been made to describe a general pattern of signs and symptoms seen in the common cold. Fox and Livingston (2) describe in great detail the pattern seen in study of colds over a seventeen-year period. Arminio and Sweet (3) recognize, through the study of 311 patients with common cold, three phases of pathological change: an initial phase, lasting 24 hours and involving extreme pallor and œdema of the nasal mucosa which exudes a watery mucoid discharge but exhibits no cellular breakdown; a second phase characterized by marked injection and redness of the nasal mucosa, with less œdema, a mucoid discharge and still no apparent breakdown of cellular structure, also lasting about 24 hours; a third phase involving complete breakdown of the cellular structure of the nasal mucosa, plus a purulent discharge, this phase lasting 4-7 days.

A great deal of evidence suggests that the common cold is, in its initial phases at any rate, an allergic response. This evidence is presented below in the discussion of the use of the antihistaminic drugs.

Agent

It was early demonstrated (4) that the common cold could be induced in human volunteers with bacteria-free filtrates of nasopharyngeal washings from patients suffering from the infection. This led to the suggestion that the aetiological agent in the common cold is a virus. Not all studies confirmed the theory (5), but subsequent work (6) did lend further strong support. Next a common cold agent was propagated in chick-embryo tissue cultures (7) and on the chorio-allantoic membrane of developing 12-day-old chick embryos (8).

Recent workers, attempting to isolate the agent of the common cold, have made use of transfer studies. Nasal washings from patients in the early stages of colds are made bacteria-free, (e.g. by filtering), and inoculated into the noses of volunteers. If the latter contract the infection, the material, known to contain a cold virus, is inoculated into hens' eggs and the eggs are incubated for a given period. The fluids of the eggs are then inoculated into the noses of volunteers. Employing this general plan, Pollard and Caplowitz (9) and Topping and Atlas (10) reported in 1947 that they had cultivated the cold virus in eggs. However, Andrewes (11) a few months later reported that a similar technique had yielded negative results. In November of 1949 Atlas reported that a strain of virus which he had propagated since 1947 had for some reason been lost.

Topping and Atlas (10) have shown, using the electron microscope, the presence of characteristic particles of the same general size as viruses of the influenza type, in egg fluids exhibiting common cold agent activity.

Contraction

A summary of the existent knowledge (12) suggests that the virus of the cold is, in a large community, constantly passing from one person to another; it usually causes no symptoms, often only abortive ones, and a real cold results only when it finds a victim whose local resistance is for some reason at a temporary low ebb. From such a person it is dispersed in greater quantity. Few people, Andrewes suggests, harbour it long; hence in isolated groups it commonly dies out quickly.

THE PREVENTION OF THE INFECTION

A great many methods have been suggested for the prevention of the common cold. The recent data on some of these methods is now to be presented.

Three Suggested Methods of Prevention

1. CONDITIONING: A number of procedures have been suggested for the purpose of conditioning the body to sudden changes in external temperature of the skin, such as cold shower baths every morning and exercise outdoors followed by hot and cold shower baths Controlled experiments by Gafafer (13) failed to show any lower incidence of colds in people who followed these practices than in a group who did not.

2. VITAMIN C: Markwell (14), after observations on hundreds of the patients of his practice in a "casual and by no means scientific" way has recommended

that ascorbic acid may be useful in common cold abortion. He suggests ¾ Gms. of ascorbic acid at the very first symptoms of cold; another similar dose after 3 ot 4 hours if needed; and another gram of the vitamin on the second and third days if the symptoms continue. In the majority of cases, the colds have been aborted. However, there was no control to the experiment.

The use of ascorbic acid with the sulpha drugs has also been suggested (15).

3. GLYCOLS: The use of triethylene glycol in the air-conditioning system of a New York bank led to the observation that the incidence of colds amongst the employees of that bank was greatly reduced (16). Bigg and Jennings worked with 640 men living in barracks of the Great Lakes Naval Training Station. Half lived in vapour-treated barracks, the control group in untreated quarters. In the second three weeks of one test there were 3 times as many minor infections in the control than in the test group. Harris and Stokes studied children in sprayed and control wards of the Children's Seashore Home in Atlantic City. In three winters of testing, the experimental group of children had 13 infections; the control group had ten times as many. On the other hand, McConnell (17) was unable to demonstrate, using triethylene glycol to sterilize room air in offices, either any reduction in the number of air-borne bacteria, or a reduction in the absentee rate, or in the incidence rate of minor respiratory illness attributable to vapour action.

Prigal et al (18) showed that propylene glycol imparts to the blood serum a specific antibiotic property which lasted in cases for 4-6 hours. This may explain a lower incidence of minor respiratory infections in subjects exposed to the vapour for only a few hours a day, as in places of work.

Old vaporizing mechanisms required air-conditioning or air-circulating systems. A newer apparatus employs an electrical clockwork to move a glycol-impregnated tape over an electrically-warmed cylinder. The cost of treating home and school rooms with this device is not great.

VACCINES

The use of vaccines for the prevention of common cold is one of the most highly contested aspects of common cold medication. A multitude of reports both for and against such treatment has been published.

In 1938 Diehl et al (19) conducted a carefully-controlled study of the value of three recommended vaccines containing a wide variety of micro-organisms commonly found in the respiratory tract. There was no evidence that vaccines, given either parenterally or by nose spray, reduce the complications of colds.

Fox and Livingston (2) on the other hand, have reported the use of a solution of hog pseudoglobin fortified by material collected from persons during the first 48 hours of an active cold. They concluded that 50% of their patients, who developed no colds for at least six months, had been successfully hyposensitized.

The fact that the pharmaceutical house which is this city's chief producer of oral vaccines admits that the preponderance of evidence is against the effectiveness of such preparations reminds one of an editorial of the Journal of the American Medical Association in 1944 (21): "Recent communications . . . indicate that the prescription and sale of cold vaccines is again taking place on a large scale. . . . The scientific evidence against the value of oral cold vaccines is

overwhelming; consequently individual physicians and firms who deal in pharmaceuticals and who lend themselves to the wholesale uncontrolled distribution of such preparations are perpetrating an unwarranted commercial assault on the public pocketbook."

Antihistaminic Drugs

A number of observations have suggested the fact that the common cold is, in its initial stages at least, an allergic phenomenon; i.e., due to the release of histamine or a histamine-like substance in the body: (*a*) The similarity in rhinitis symptoms of an acute head cold and allergic states; (*b*) The presence of a greater concentration of histamine or histaminic substances in the nasal secretions of individuals with colds than in those of persons with allergic rhinitis (22) (23); (*c*) The production of symptoms similar to those met in the early stages of common cold by spraying histamine on the nasal mucosae of non-allergic individuals (24); (*d*) The development in cold transfer experiments of more severe symptoms in allergic than in non-allergic patients (2); (*e*) An eosinophilia in the nasal smears of 42.6% of 96 patients during the initial 24 hours of a cold (3). (Allergic individuals generally exhibit eosinophilia).

For these reasons it has appeared worthwhile to attempt to abort the common cold by the use of drugs which are known to be specifically antihistaminic in action.

Brewster (26) treated more than 100 patients with Benadryl. Of patients in whom treatment was begun within the first hour of onset of symptoms 90% were cured. Treatment within 6 hours of onset of symptoms gave cure in 74% of cases. Results in controls with codeine sulphate and papaverine hydrochloride were much less favorable. Because of these observations Brewster postulated that a cold begins as an allergic reaction. A trigger mechanism (chilling, ingestion of food or drink to which one is sensitive) initiates an allergic reaction which causes localized œdema of the mucous membrane. The normal protective power of the mucous membrane is decreased, so that the cold virus, if then present, makes a successful invasion. The pathogenic organisms normally present in the respiratory tract cause the complications of the common cold.

Benadryl, however, had the side-effect of making too many patients sleepy, and could not be made available to the public.

Murray (27) treated 494 patients with 50 mg. tablets of Pyribenzamine. Of these, 314 were made symptomless within 3 days. In 83 there seemed to be some lessening of symptoms. So in 75% of cases there was improvement. In this case, again, there was a high incidence of sleepiness.

Arminio and Sweet (3) tested the effect of Neohetramine (thonzylamine hydrochloride) in the prevention of common cold when given in daily doses over an appreciable length of time. Amongst a group of 600 convent Sisters and seminary students, there were established three test groups of 100 each, receiving 50 mg. tablets of Neohetramine once, twice and three times daily, respectively, and a control group of 300 receiving no medication. The experiment was carried out over a period of 6 months. By the end of that time, in the groups receiving medication once, twice and three times daily, there had been 83%, 90% and 92% respectively, entirely free of cold symptoms. In the control group of 300 patients, only 20% had remained symptom-free. Also, the colds

of those receiving medication twice and three times daily were aborted in 13 of 18 cases in the first stage of development; whereas all colds in the untreated group advanced to the second stage, and 179 of 241 went on to the third, purulent stage.

During the six months there was no evidence of undesirable side-effects, consequently it was concluded that there are no toxic manifestations of Neohetramine.

Philips and Fishbein (28) conducted a study to determine the efficacy of a compound containing an antihistaminic drug, chlorothen citrate (25 mg.), acetophenetidin (320 mg.) and caffeine (32 mg.). The acetophenetidin and the caffeine were present for analgesic and antipyretic action, the caffeine also to counteract any sedative effect. In 92 persons treated with the product, the average duration of colds was 2.7 days as compared with 5.3 in 74 treated with aspirin. Early administration was seen to be important. The compound may be administered with safety within the dosage levels prescribed because of the low incidence of toxic effects (only two patients showed evidence of some dizziness).

As a result of the work described, many pharmaceutical houses have claimed the antihistamines to be the panacea of common cold prophylaxis and treatment. Because certain of these drugs have been made available without prescription, the National Better Business Bureau of America recently initiated an inquiry into the question. This resulted in a warning to the public against possible side-effects of the drugs, particularly in the case of small children. The American Medical Association Council on Pharmacy and Chemistry has recently said: "Experience with these drugs is not yet long enough to know whether or not they are harmless when used over long periods of time. Furthermore, the amounts taken in persistent colds may be definitely beyond what has been established as safe." The only drug at present which might challenge this statement is Neohetramine, for which continued dosage in common cold therapy has been reported (as described above).

Schwartz (35) has compared the effectiveness of several antihistaminics in patients exhibiting various allergic symptoms, and has also noted their relative toxicities and number of side effects. Working with Benadryl, Pyribenzamine, Neo-antergan, Antistine, Histadyl and Neohetramine, he showed that all were essentially equally effective (with Benadryl and Antistine somewhat less so). The order of decreasing toxicity is that in which the drugs are listed above. In the case of Neohetramine only 7.2% of 111 cases exhibited side-reactions, and all such effects were mild ones.

COMMON COLD THERAPY

An old adage suggests that there is only one way to treat the common cold —with contempt. Despite this fact, there exist at present probably as many recommended cures for cold as there are susceptible people. It has been pointed out, with partial if not complete accuracy, that a good number of otherwise rational physicians will revert, in the cases of their own common colds, to the tried and probably untrue therapies of grandmothers and great-aunts. The common cold is in this respect a close relative to the hiccough.

There now follows a review of some of the more recently published work concerning cold therapy.

1. Sulphonamides and Penicillin

Studies of the effectiveness of the sulphonamides in treatment of common cold have led to the conclusion that these drugs have little if any effect on the symptoms of a mild cold. However, their use is indicated in cases wherein a severe secondary infection threatens to develop.

Feinfield and Collen (31) conducted a study of the effect of penicillin in the treatment of the common cold in ambulatory patients. In a small, controlled group of subjects with uncomplicated colds, the use of 400,000 units of oral penicillin daily for four days had no significant effect on the clinical course of the treated subjects as compared with those of the control group.

The belief is held by some that penicillin should be used only when danger of serious infection is present. It is suggested that employing it for minor conditions will sensitize the patient towards it, eliminating it from subsequent use when it is more seriously required (32).

2. Vasoconstrictors

Various preparations containing vasoconstrictor principles have been marketed. These are in the form of aqueous solutions of various ephedrine-like compounds, emulsions, oil solutions, jellies, inhalers, and preparations combining vasoconstrictors with sulphonamides or with antibiotics. An effective summary of the use of such preparations has been prepared (32). Such drugs serve to maintain patency of the nasal passages, and may reduce the degree of initial injury to tissues which results from intense congestion (32). It is suggested that vasoconstrictive measures be employed during the acute stages of a cold, but no oftener than every four hours (33). Excess use leads to irritation of the nasal tissues. Others opine that vasoconstrictors rarely give appreciable relief of nasal obstruction and may even interfere with nutrition of the tissues of the nasopharynx.

3. Diet

Special diets have been advanced from time to time for either prevention or cure of colds. Most commonly suggested are diets of high protein, of low carbohydrate, and diets containing large quantities of citrus foods. None of these theories is supported by carefully-controlled studies. Widespread is the belief that use of sodium bicarbonate or other antacid is a preventive in the treatment of common cold. However, Diehl (29) has shown conclusively that results obtained by "alkalinization" are of little or no value.

4. Antihistaminic Drugs

Arminio and Sweet (3) studied the effect of Neohetramine in the therapy of the common cold. Their results indicated an abortion of colds in the great majority of members of the test group over those of effective controls. The effectiveness of the drugs becomes less as the duration of the cold increases. The usefulness of antihistaminics, then, is indicated in both prevention and therapy of the common cold.

5. Miscellaneous

(*a*) Hitschler *et al* (30) have recently used human serum immune globin intranasally by local instillation for the purpose of determining its effect on the common cold. This was done because, since antibodies specific for other viruses have been found in human gamma-globulin, it was reasoned that this fraction might cause immunization, when applied locally, to the common cold. However, objective criteria in the study

of test and control groups amongst 70 children indicated no apparent effect of gamma-globulin in therapy by the method employed.

(*b*) Randolph (25) has suggested that the habit of nose-blowing must be broken. The practice creates a positive pressure in the upper respiratory passages which forces secretions back into the sinuses, causing the normal excretory mechanism by means of cilia to fail. This leads to plugging of the sinuses. Forceful inhation, however, creates a negative pressure and helps draw the secretions out. This, he says, is an important method of aiding the natural excretory processes, during the common cold.

SUMMARY

The recent publications on the subject of the common cold are reviewed. The evidence they present is considered under three main categories.

1. Nature, Agent and Contraction

(*a*) Differentiation of various infections of the upper respiratory tract is difficult.

Three successive general stages have been recognized in the symptoms of patients with common cold.

(*b*) The agent of the common cold is a virus. Attempts at its isolation, making use of transfer studies, have in some cases been reported as successful, in others unsuccessful.

(*c*) The agent, it seems likely, is, in large communities, constantly passing from person to person. However, symptoms result only in those cases in which the local resistance of the individual is for some reason low.

2. Prevention

(*a*) Morning showers and outdoor exercises have shown no appreciable value in cold prevention.

(*b*) An uncontrolled experiment suggests that ascorbic acid (Vitamin C) will abort colds in the early stages.

(*c*) Glycol vapours seem to be of value in lowering cold incidence by sterilizing air. Glycols may have the ability to impart to the blood an antibiotic proper- which lasts for 4-6 hours.

(*d*) The great preponderance of information suggests that vaccines are of little use in common cold prevention.

(*e*) The common cold is an allergic phenomenon in its initial phases. Strong evidence supports the value of antihistaminic drugs for abortion of colds in their early stages.

3. Therapy

(*a*) The sulphonamides are best used for common colds only when serious secondary infection threatens.

A controlled experiment could exhibit no significant effect of 400,000 units of penicillin, taken daily, on the symptoms of mild colds. There is some fear that frequent use of penicillin will lead to sensitization to it, prohibiting its use when more seriously needed.

(*b*) Various vasoconstrictor preparations exist. These are useful, but caution must be exercised to avoid irritation of the nasal mucosa.

(*c*) Antihistaminic drugs have been shown to be of value in therapy of the common cold, their effectiveness decreasing as the duration of the cold increases.

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THE INTESTINAL ABSORPTION OF NEUTRAL FAT*

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MANY YEARS AGO, it was agreed by most medical scientists that the mechanism of fat absorption was at last understood. After many active decades of brilliant investigation and heated discussion, it must have been a satisfying experience. And now, today, with a century's efforts behind us, combining the contributions of many of the world's eminent phyiologists, the entire process is a complete mystery. True, there are several theories offered to explain the various steps undergone by fat from its ingestion to its initial deposition after leaving the intestine, and each of these in turn has reversed current opinion and has been deemed the solution to the problem. But not one explains satisfactorily all the experimental observations, and important pieces of evidence for most of them have not proven reproducible.

Prior to an examination of the mechanism of fat absorption itself, a few introductory anatomical observations will be made. The one structure inseparably associated with fat absorption is the intestinal villus, through the columnar epithelium of which all fat passes as it leaves the intestinal lumen. This passage is most active at the tips of the villi, and does not occur at all in the crypts of Lieberkühn between them. Deep to the epithelium lies the connective tissue core with its rich capillary rete supplied by one or two arterioles depending on the species. Here also, along with a ribbon or two of smooth muscle, are the central lacteals, the blind initial twigs of the lymphatic tree. These drain past valves into the submucosal plexus whence the familiar lymphatics course through the mesentery. After these traverse the main mesenteric lymph nodes at the root of the mesentery, which are relatively large in the rat, the intestinal lymph trunk is formed which joins the thoracic duct. Now, although the entire small intestine contains these villi, triglyceride absorption, in the rat at least, is not uniform throughout its length. We have found absorption restricted to the portion distal to the ampulla of Vater and maximal in the middle third. Distal to this again, activity falls to nil in the terminal ileum. Although gastric fat absorption has been claimed, it is generally agreed nowadays that any absorption from the stomach is negligible. We have not seen absorption from the colon.

Having acquainted ourselves in a general way with these anatomical facts, let us consider briefly the history of the experimental work in this field. In 1851, Brücke proposed absorption of fat in a bile-stabilized emulsion. Zawaryken in 1885 suggested absorption by phagocytosis, a theory amply disproved. Heidenhain in 1888 claimed that the products of lipolysis dissolved in the cell membrane to enter the epi-

*Compounds such as olive oil which contain glycerol bound to three fatty acid such as oleic acid:

CH_2-O—fatty acid
CH -O—fatty acid
CH_2-O—fatty acid

†Banting and Best Department of Medical Research. This paper is modified from a lecture given before the Toronto Physiological Society January 31, 1949.

thelium, a mechanism now known to be possible in invertebrates. In 1900 Pflüger argued that fats were absorbed as soaps. Kischensky in 1902 thought that fat entered the gut wall by slipping between cells. In 1936, Verzàr published a monograph in which he attempted to show that triglycerides are totally split to fatty acids, which are absorbed as a water soluble complex with bile. These fatty acids are then resynthesized to neutral fats and carried away in the lymph. More recently, Frazer has proposed that triglycerides need not be broken down to fatty acids and glycerol to be absorbed, but that they can enter the villi as particles and thence be transported in the lymph. Fatty acids, on the other hand, he claims, are absorbed dissolved in the aqueous phase and are swept away in the portal blood.

In evaluating these theories, it is convenient to consider fat absorption under these headings: (*a*) processes occurring in the intestinal lumen (*b*) the passage of fat through the epithelial cell membrane (*c*) processes in the villus epithelium (*d*) the removal of fat from the epithelium to the core of the villus and its transportation from the intestine.

Of the processes taking place in the lumen, lipolysis, or the removal of the fatty acids from the neutral fat molecule, must first be considered. According to Verzàr, neutral fats are totally broken down. As evidence for this, he states that if groups of animals are fed olive oil, oleic acid, or sodium oleate (soap), no histological difference in the appearance of the intestinal fat can be demonstrated between the groups. Presumably then, the same substance is entering the cells in each case, namely, fatty acids. Hence, triglyceride must be broken down to fatty acid for absorption. Frazer, as will be mentioned below, disagrees with these observations. Verzàr also points out that simple glycerol-esters are broken down in the lumen of the intestine and that free glycerol is found in the lymph after meals. But results with esters need not apply to neutral fats and none of these or similar experiments proves that neutral fats are *completely* split into their component parts. Many workers imagined that if they fed animals a fat stained red (for example with sudan) and at autopsy saw red fat in the fresh tissues, they would have proven that the fat they fed had not been broken down for absorption. But since the dye associates with the fatty acid component of the neutral fat and remains with it whether lepolysis occurs or not, their assumption was unfounded. Nevertheless, Verzàr argued that if red fat could *not* be found in the fresh tissues at autopsy, then surely fat could not be absorbed unsplit. We have been unable to agree with his claim that such is the case in rats, for we have seen red fat in the intestine, lymph nodes, and fat depots.

Frazer, on the other hand, claims to have proven that the neutral fat molecule can be absorbed without being completely broken down. He claims that fine emulsions of paraffin can enter the villi and that, if such is the case, since no known chemical changes can alter paraffin in the intestinal lumen, and since it cannot be rendered water-soluble, it must be absorbed unchanged, that is in the form of particles. If this obtains for paraffin, he continues, then neutral fat should also be capable of particulate absorption, and need not be split. However, recent work has been absolutely unable to verify these claims of Frazer's.(1) Frazer has also stated that, histologically, the amount, disper-

sion, and distribution, of lipids in the villi of rats fed olive oil differed from that seen in rats fed oleic acid. This observation is in direct opposition to that of Veraàr's mentioned above. Frazer took this to mean that a different lipid entered the cells in each case,—unsplit neutral fat in one, fatty acid in the other. Upon repeating this experiment we have found essentially no histological difference such as Frazer describes between the two groups, although the absorption of fatty acid was slightly delayed and less active. Still further evidence has been advanced by Frazer in support of his particulate absorption theory. In his laboratory and elsewhere it has been demonstrated that pancreatic lipolysis in vitro ceases when only 30% of the fatty acids have been liberated from the neutral fats. He believes that this is due to blockage of the lipase by the deposition of the freed water-insoluble fatty acids on the oil-water interface of the emulsion in the reaction medium. Water soluble fatty acids, rare in foods, should not settle on the interface, he argues, and hence should be totally split off; this is said to be the case with tributyrin. Frazer states that the addition of more lipase or more fat does not increase the percentage of fatty acids freed and that, although large amounts of fatty acid and mono- and diglycerides could be recovered from the reaction mixture in the first five hours, no free glycerol could be found. Since the first five hours sees most of the fat absorbed, in vivo, he presents these points as proof that fats must be absorbed as mono-, di-, or triglycerides. Nevertheless, there is no reason for believing that his results obtained in vitro apply to the living animal, and, to date, in vivo confirmation is inadequate.

Following lipolysis, some means must be found to prepare the fat for entry into the epithelial cells of the villi. If soaps can exist in the intestinal lumen, they should be able to enter the cells in aqueous solution. Verzàr denied the existence of soaps in the chyme of the small intestine because he believed it too acid (pH-6.5). Schmidt-Nielsen, however, has shown that at pH 6.5 sufficient soap can exist to permit absorption in this form.(2) Verzàr considered that bile was essential for fat absorption, and presented convincing evidence that the fatty acids derived from complete splitting of the ingested fats formed water soluble compounds with conjugated bile salts (containing glycine or taurine). These were then free to enter the cells in the aqueous phase. In the absence of glycine or taurine the solubilizing action of bile salt was lost at the intestinal pH. But Verzàr found that the liver did not secrete sufficient bile salt to dissolve all the fatty acids absorbed; accordingly he postulated a bucket brigade mechanism whereby the fatty acid was carried into the epithelium in the bile salt complex where it was released, allowing the bile salt to return to the lumen for further duty.

If, on the other hand, one believes, as Frazer does, that fat is absorbed without being entirely degraded to fatty acid and glycerol, a different arrangement must be located to permit the entrance of unsplit fat into the epithelium. Because glyceride fat cannot be rendered water-soluble by any known system in the intestinal lumen, Frazer decided that it must enter in particulate form, that is as an emulsion. The only system producing a suitable emulsion which would form spontaneously, remain stable in the gut, and utilize materials

present in chyme was that of fatty acid, bile salt, and monoglyceride,—at least according to Frazer. He describes some evidence which he believes shows that this emulsifying system is in fact functioning in the intestinal lumen. He does not attempt to explain how long chain fatty acids, which are quite insoluble in aqueous solution, but which are certainly readily absorbed, are prepared for absorption.

The next stage to be considered is the actual passage of fat through the cell membrane of the villus epithelium for which the processes in the lumen have paved the way. This phase can be studied only indirectly. When fat first begins to accumulate in the epithelium it does so as fine droplets close to the outer nuclear poles; it then gradually appears in the cytoplasm between the nucleus and the luminal border of the cell, coalescing into large globules which soon occupy this whole space. But there is always a narrow fat free zone adjoining the intestinal lumen which was named from its microscopic appearance the "brush" or "striated border" by the older histologists, and which has served as the centre of discussion on the entry of fat into the epithelium ever since. Verzàr wrote that fat passed through this zone in aqueous solution and claimed that in such a form it would not take fat stains: hence the fat-free striated border. According to Frazer, as has been mentioned, fat must traverse the cell membrane as particles. He therefore argues that the striations seen in the brush border represent pores 0.5μ in diameter in the cell membrane, basing his views on the results of cytological studies and reported observations of fat droplets within the "pores." He lists as further evidence that the fat particle size found in the intestinal lumen and in his artificial emulsions containing fatty acid, bile, and monoglyceride, as well as the diameter of the "pores" in the brush border are all computed to be 0.5μ, and furthermore that paraffin emulsions are absorbed when the particle size is less than 0.5μ. It has been mentioned above that this latter observation has been strongly challenged. He then states that, obviously, if two groups of rats are fed stained olive oil and stained oleic acid respectively, and if all the oil is broken down in the process of absorption to oleic acid and glycerol, then there should be no demonstrable differences between the two groups. He goes on to claim that he has found histological differences. We have been unable to agree with this claim. He also claims that the fate of the absorbed lipid differs in the two groups; again, as described below, we cannot agree. Nevertheless in view of these supposed differences, Frazer reasoned that different lipids were entering the cells of the two groups of rats,—fatty acid in the one, glycerides in the other, presumably in particle form.(3) He has also included the results of experiments with adrenalectomized rats into his theory.(4) Doubly adrenalectomized rats have been found to absorb free fatty acids normally but only 60% of neutral fats (normal, 100%). But if tributyrin, a neutral fat with water-soluble fatty acid, is fed, absorption is stated to be normal. Since adequate salt therapy, as well as A.C.H., corrects defective neutral fat absorption after adrenalectomy, Frazer concludes that proper electrolyte balance is essential for triglyceride, but not fatty acid, absorption. This conclusion, he believes, is in accord with a particulate theory of neutral fat absorption because the particles, carrying a negative charge,

must pass through pores in the cell membrane. As explained previously, since tributyrin can be split entirely by pancreatic lipase, Frazer claims that it is not absorbed as particles; this, he states, is the reason that it enters the cells normally following adrenalectomy. Now all this portion of his reasoning, constituting the essence of his theory of fat absorption, depends on the presence of pores in the "striated border" of the intestinal epithelium. But the nature of the brush border cannot be clearly seen with the light microscope, and the striated appearance could result from the presence of cilia-like structures as well as of pores in the periphery of the cells. Indeed, in the larval frog true cilia occur, while in the adult, the usual "striated border" is seen. The whole matter seems to have been decided, however, by recent work with the electron microscope which shows that the "striated border" contains projecting structures embedded in the protoplasm, *but no pores.*(5) There appears to be, then, no explanation of how particles could enter the epithelial cells, and it appears that we must reject Frazer's particulate theory of fat absorption.

Having completed our discussion of the passage of fat into the intestinal epithelium, we shall now consider processes taking place in these cells. Fats, according to Verzàr, must be totally split to enter the cells, so that the food fats in the epithelium are in the form of fatty acids. But, in lymph, he states, they are largely in triglyceride form; hence resynthesis must occur. Jeker has provided histochemical evidence that this reaction goes on in the epithelium. Chemical evidence is profuse but inconclusive. In this resynthetic process, Verzàr held that phosphorylation was important and there is some evidence for this including a recent histochemical study. (6) He was led to this conclusion when he discovered that poisoning with phlorizin or iodoacetate, both of which he considered inhibitors of phosphorylation from his work with carbohydrate metabolism, resulted in impaired fat absorption. Since he also found impairment of fat absorption after adrenalectomy, he decided that phosphorylation depended on the presence of A.C.H. Unfortunately, it has since been shown that the dose of poison which he used actually destroyed the mucous membrane and that the impaired absorption after adrenalectomy can be prevented by correcting the resulting electrolyte imbalance. Phosphorylation in fat absorption is receiving considerable attention at present but the field is very confused. Only the work of Barnes et al will be mentioned. These workers, using an ingenious labelling technique, showed that virtually none of the fatty acids of the phospholipids in the intestinal mucosa was replaced by ingested fatty acids, while half those in the neutral fats of the epithelium was replaced.(7, 8) It would appear, then, that phospholipids do not play the rôle of an intermediary in fat absorption.

Now if glyceride can be absorbed unsplit, as Frazer claims it can, resynthesis in the epithelium is not important. Nevertheless, he does not indicate the fate of the fatty acids and lower glycerides which must, according to his theory, appear in the epithelium. Phospholipids are regarded by Frazer as useful fatty acid carriers and as stabilizers of the chylomicra in blood and lymph.

Miscellaneous observations on the intercellular phase of fat absorption include the demonstration by Cramer and Ludford that the Golgi apparatus plays

a rôle in fat absorption, which we have reproduced. These authors also reported that B vitamins facilitated the absorption of fat. Frazer, in turn, has claimed that choline, but not the B vitamins, improves fat absorption, and that, as a result of this effect, it is possible, histologically, to distinguish between the intestine of rats fed fat plus choline and those fed fat alone. Although we have investigated this latter possibility exhaustively, we have been entirely unable to reproduce these morphological findings.(9) Frazer, by chemical studies (10), and, recently, Tidwell, by chylomicron counts (11), have provided evidence that choline increases the rate of fat absorption. Tidwell suggests that this activity of choline is bound up with the formation of phopholipids during fat absorption.

We now pass to the final phase of fat absorption, the transport of fat out of the intestinal epithelium to the rest of the body. No special theory has been offered to explain the passage of fat out of the epithelial cells, although the passage of fat from the lumen of the intestine into these cells has been vigorously discussed for over a century. We have seen the formation of fat pools between the epithelial cells as soon as the latter are filled. These pools overflow into the intercellular spaces of the villuis core, enter the lacteals somehow, and traverse the lymphatic tree. Contraction of the villi undoubtedly plays a rôle here.

That fat is carried away from the intestine in the lymph is accepted by all; however, the *proportion* of absorbed fat carried by this route is disputed. Many experiments, often openly fallacious, can be quoted which purport to prove that absorbed fat is also carried in the portal blood; others deny it. Lymphaticovenous connections involving the portal vein may cause some of the discrepancy. Verzàr believed that fat in the villus core was in particulate form and hence was incapable at traversing the walls of capillaries. He therefore taught that all fat was absorbed in the lymph. But Frazer claims to have traced absorbed lipids, (by staining them before feeding and by counting chylomicra), through the portal blood to the liver, but not through systemic blood (from the thoracic duct) to the fat depots, after giving animals meals of oleic acid. Following meals of stained olive oil, he states that he has traced the fat through the systemic blood to the depots, but not through the portal blood to the liver.(3) No photographic evidence for these claims has been published, however. And Tidwell (11) by counting chylomicra, has found the absorbed lipids in systemic blood at the same level after feeding either olive oil or the fatty acids obtained from olive oil. When we repeated Frazer's experiments, we never found ingested fat in the portal blood or liver, but after feeding *either* stained oleic acid *or* olive oil, we observed that the mesenteric lymph nodes and the fat depots contained ingested lipids to the same degree in each case. Moreover, after ligating the intestinal lymph trunk and then feeding *either* oleic acid *or* olive oil, we found that the central lacteals of the villi, the intestinal lymphatics, and the mesenteric lymph nodes were enormously distended with fat-laden lymph. In both groups the quanity of dammed up fat was the same. We must insist, therefore, that after meals of *both* neutral fat *and* fatty acid, absorption occurs through the lymphatics, and to about the same extent in each case. Finally, although previous work has indicated

that only 17-60% of ingested fat can be recovered from lymph, in experiments now in progress at the Mayo Clinic, Bollman et al are finding a 100% recovery of absorbed olive oil *and oleic acid* from the lymph. Their success is due to a superb technique by which they collect the lymph from an exteriorized plastic tube inserted in the intestinal lymph trunk of a rat held immobile in a special holder.(12) We are at present studying the part played by the lymph in fat absorption using a modification of their technique whereby the lymph can be obtained from normally active rats. It appears, therefore, that we cannot accept Frazer's partition theory of fat absorption; both neutral fats and fatty acids are absorbed entirely in the lymph.

This concludes the discussion of the experimental work in the field of neutral fat absorption. Although, at the present time, fat absorption is still largely a mystery, the following tentative outline if offered as seeming the most probable. Ingested fats reach the small intestine. Possibly with the aid of bile, they are emulsified, and on this emulsion pancreatic lipase acts, releasing fatty acids. A small proportion of these are converted to soaps and absorbed in aqueous solution. By the action of the Mass Law, more soap forms to replace that absorbed, until all the fatty acid has entered the epithelium. Bile salt may also act in dissolving fatty acid in aqueous solution. If fatty acids are fed, they are solubilized and absorbed directly. This absorption is most active in the middle third of the small intestine. The glycerol remaining after the fatty acids have been split off the neutral fat molecule dissolves in water and is absorbed. Within the epithelial cells the soaps are reconstructed to triglycerides. Almost certainly, other intracellular reactions, possibly phosphorylation, are involved in both the passage of fat into the epithelium and the resynthesis of neutral fats. Somehow, the resynthesized neutral fats pass out into the spaces between adjacent epithelial cells, forming pools which overflow into the villus core. In some way, this fat enters the central lacteals, probably aided by villus contraction, and traverses the lymphatic tree taking on the form of chylomicra. Through the thoracic duct, the systemic circulation is reached, and the absorbed fat is deposited in the fat depots, by means unknown. It is also unknown whether the absorbed fat passes through the hepatic cells, perhaps undergoing alteration, before it reaches the fat depots.

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"ARE YOU ON THE SUCKER LIST?"

G. McL. WILSON, M.D., F.I.C.S.(A)

Occupying number one position on any national "Sucker List", is the Medical Profession. This group of 16,000 to 18,000 professional men, theoretically in the higher income bracket, is a rich lode that is profitably mined by salesmen of all descriptions, representing almost every conceivable scheme that was ever calculated to make money fast. Not a day passes but brochures from some company or appliance manufacturer come into the office, describing in glowing terms the merit and quick return on the investment of a thousand or so dollars. In addition, salesmen of insurance companies will camp on the doorstep in droves (but be sure to buy your insurance from an experienced and far sighted agent who has a reputation for looking after his clients in the future and who can plan their insurance intelligently).

The purpose of this article is to give the embryo practitioner some conception of what he will need in his office in the way of equipment and furnishings, and more particularly to help him avoid purchasing many things which look imposing and scientific but are actually of little or no practical value to him. It should be understood that this is not an indictment against the more reputable equipment and instrument houses; but unfortunately, not all are reputable, particularly in their sales force; and if the young practitioner is not careful, he will find himself loaded down with equipment he will seldom use, as the result of an interview with a silver tongued salesman.

The young doctor on entering private general practice will find himself generally in one of three categories. Firstly, as an assistant to an established practitioner, usually an older man who has gone through this period himself. Secondly, as a junior member of a group whose equipment is already on hand; and thirdly, as an optimistic energetic practitioner starting on his own, determined that his practice shall be of the most modern type available. It is this latter group that should take particular heed of the following remarks.

What are the basic physical requirements for setting up a Practice?

Location. This is first in importance. It would appear that the young practitioner would make a mistake in setting up his office in a large downtown office building, where he is simply one more unknown ant in the ant-hill. The trend these days is to decentralization, and this is equally true in the practice of medicine. Thus you will see, in most large centres, doctor's offices growing up throughout the suburban districts.

He must give thought, in picking out his office location, to the nearness of a pharmacy, and the availability of parking space for patients' cars. He must find out if the thoroughfare on which he is proposing to locate is noisy; if there is much electrical high tension interference and if the acoustical properties of the building are good, for there is nothing more disturbing to a patient or to a doctor examining a patient, than a noisy, reverberating building. Has the proposed office suite sufficient ventilation for summer use and adequate heat in the winter time? Is the space available going to prove sufficient in the future?

If the office is located on the second floor, in the absence of elevator service, are the stairs easily pitched or are they steep and difficult to climb? Is the proposed waiting room bright and airy? There is nothing that discourages a patient from returning to a physician so much as having to face a hard flight of stairs or a dingy, dull and cramped waiting room.

The young practitioner now will glance at his bank book, probably gulp and then head for the nearest instrument house, where he will learn that the acquisition of even the bare adequacies of equipment and furnishings are going to be far more costly than he, even in his most pessimistic moments, ever imagined. However, there are various ways to circumvent this particular problem. The first is not to be misled by bright, shiny, new and probably costly equipment. Less ostentatious and less fancy articles will do the work equally well, at least for a start, and there is actually a psychological advantage to the younger physician in being surrounded by articles which have acquired a mellowness through use and age.

Consulting room furnishings. A desk of moderate proportions with a locking drawer and good conservative design, is the first thing. It is a mistake to buy anything except the best available for his own desk chair, as he will spend a good part of his life sitting therein. A minimum of two comfortable, preferably leather upholstered chairs for his patients are also a must, and it is probably wise to consider the purchase of a good grade carpet, if the office is not so equipped. Good quality drapes of a conservative design, venetian blinds if the office has not got them and two or three well chosen pictures for the wall will complete all that is necessary for his consulting room. The writer has laid more stress on this particular room and has chosen it first, because it is in this environment that the practitioner must sell himself and his ability to his patients, and if he is surrounded by an environment of dignity and good taste, his own self-confidence will be unconsciously increased and the impression upon the patient will be beneficial.

Office nurse. The next most important thing in equipping an office is the choice of a medical stenographer and office nurse. The practitioner must remember that it is his office nurse who makes the first contact with the patient, and as patients are generally people either mentally or physically ill, they are much more alert to first impressions and are more greatly swayed by them than is the average person.

I have spoken purposely of the choice of an office nurse before the problem of the waiting room, because, if the practitioner is wise, he will allow the fresh and natural enthusiasm of the girl who is to handle a lot of his responsibility, to have a hand and a say in the decorating and equipping of the all important waiting room. The ideal office nurse is an amalgamation of many accomplishments. She must be of neat and attractive appearance and of dignified and courteous manner. She must have a basic interest in people. She must be placid and must be able to deal quickly and accurately with difficult situations. She should have some knowledge of the nursing profession and the nervous and emotional strain under which the doctor works most of the time. She should have some bookkeeping ability and must be a neat and accurate typist. Her previous experience in a doctors office is desirable but not necessary as it is a simple thing to teach an intelligent girl

the basic essentials of office nursing. Neatness, cleanliness and an appreciation of the meaning of the word sterile are basic—the rest can readily be learned.

The waiting room—mecca of dead cigar butts, spilled ashes, torn magazines, horsehair sofas, staleness of atmosphere and dusty diplomas hung askew on the walls. If there was ever a formula to ensure penury in medical practice today, it is outlined in the previous sentence. The waiting room is the patients' first introduction to the office and must instill a sense of the personality of the doctor himself. The furnishings should be comfortable, in good taste, simple and cheerful. It should approach as closely to one's living room as is practical, for the average patient over a period of months, will spend a considerable amount of time in this room. The pictures on the walls should be in good taste, simply framed, and the decorations and furnishings harmoniously chosen. This does not imply the expenditure of a lot of money. There must be an adequate number of ash trays. One or two low tables for magazines as well as magazine racks are necessary, and the lighting should be indirect and non-glaring. In other words, the waiting room should be furnished as a room in one's own home.

If the design of the office will allow it, the provision of an alcove for the office nurse is desirable as it will allow her access to the waiting room and also to the consulting room and examining room. It will keep her files and confidential documents out of the way of inquisitive eyes and it is amazing how inquisitive those eyes can sometimes be. She should have a cash drawer which can and should be locked at all times when she is not actually at the desk. While the noiseless variety of typewriter is not too popular with stenographers, it is certainly valuable in a doctor's office. It is advisable to have the ceiling over this particular area lined with some type of acoustic tile, to absorb excessive typewriter clatter. The telephone bell in the consulting room should be disconnected, and all calls taken by the nurse, who, in turn, will call the doctor by a buzzer if he must answer the phone himself.

Filing System and Ledgers. The reader may be amazed that so far not a single item of apparatus has been discussed. Quite frankly a practice can be carried out with a minimum of instruments and equipment, but everything mentioned previously is a necessity these days. I do not believe that it is a hard-boiled statement to make that in the medical profession, as in other lines of endeavour, a workman is worthy of his hire. For this reason, it is important to keep extremely accurate records, not only of patients' ailments and visits but also of the work that is done. There are a number of good systems available, but the simpler ones probably are better for everyone concerned. In a large clinic, the use of a double entry system with individual ledger sheets for each patient is an absolute must, but in individual practice the so-called double envelope system with a control ledger and day book is sufficient. In the double envelope system there is a compartment for a charge sheet and another for the cards or sheets containing the case history. The control ledger is entered up from the day sheet or day book and the accounts payable ledger is balanced against the receipts for all disbursements. This is of vital importance around the end of March! Mr. Abbott and his genial inquisitors have a mania for checking into receipts for alleged disbursements! The office nurse must be

imbued with the realization that her salary depends, to a very large extent, on how accurately she keeps records of the patients addresses and business connections. The majority of the people are in a constant state of movement, and addresses, phone numbers, etc., are changing continually. Even to the point of boredom, she should courteously, but firmly, enquire of the patient each visit as to his address, if the visits are more than a month apart. There is no use doing three or four hundred dollars worth of work on Mrs. John Doe, if her address is unknown when it comes time to send her account. The cost of living is so high and the cost of operating an office has risen so greatly that, in order to survive financially, the physician must pay attention to these matters as was never necessary a generation ago.

The Examining Room. Large or small, this room must be scrupulously clean, redecorated at least twice a year and all exposed enamelled surfaces painted even more frequently. It must be spotless at all times. What is the basic equipment for this room? An examining table of the readily obtainable, more compact type, with extention foot rests and an extention shelf at the bottom, is first. It takes up less room and is more compact and useful than the older six foot, non-collapsible type. It should have several drawers at the foot to contain the necessary instruments when doing vaginal examinations. It should have an electrical outlet and the head end of the table should be adjustable to semi-Fowler's position. An adequate linen supply must be available, and in most larger centres it is probably more practical to subscribe to one of the linen supply dealers who will keep a constant stock of fresh mended linens available in the office. A monel-metal-topped, wheeled instrument tray is nice, but is not essential. With a little care, and if the room is not too large, shelves may be built in, which will serve quite adequately. The examining room should have a good, light-proof blind with light traps in which it travels, in order that the room may be adequately darkened for various ophthalmoscopic and transillumination procedures. It should be extremely well ventilated for there is nothing more depressing than the smell of cauterized tissue or high body odours lingering in an examining room after one patient has departed. The use of an air purifier is advisable. If no provision has been made for ventilation, an exhaust fan to the outside, located near the ceiling, should be installed, despite the expense.

Basic Equipment.

(*a*) Diagnostic. This should include a sturdy mercury-type sphygmomanometer; an ophthalmoscope and a diagnostic ear, nose and throat set; at least three vaginal speculæ, either of the Simm's or Duckbilled type, whichever you prefer, and particularly one so-called junior size for nulliparæ and unmarried women.

I believe that every physician should know how to use and should own a protoscope and a sigmoidoscope. These instruments, which may be purchased reasonably from the National Company, are interchangeable and can be used, together with their efficient headlight, from the main transformer. Another accessory to this transformer which is extremely valuable is the electrocautery.

An oto-laryngoscopy set is necessary and a set of uretheral sounds is likewise valuable.

The usual minor laboratory equipment—test tubes, slides and slide covers,

spirit lamp, and the simpler stains including Pappenheim's stain should be included. The valuable and non-critical Pappenheim's stain is, next to Gram's stain, the most useful in demonstrating Gram-negative Diplococci. Wright's blood stain and Loeffler's stain are, of course, standard. The usual tests for sugar are also standard. Some diabetic clinics are placing more reliance in the results obtained from the Clinitest tablet than from the Benedict's reducing solution. One further instrument that might be well used and probably should be purchased at the outset is a Basket biopsy forcep, for removing sections of cervix or other areas for further study. The public is very cancer conscious these days.

(*b*) Therapeutic. Bandage scissors, preferably attached by a chain to the adhesive dispenser, are very useful and this arrangement keeps them handy. One or two simple nasal instruments are valuable and, particularly, a long-nosed, foreign body extractor will earn its keep many times over during its lifetime. If you are able to remove a marble or a cherry pip from little Johnny's nostril without undue trauma, you have won that family as patients for keeps. The same can be said for Sliver Removing Forceps. A couple of scalpel handles of the smaller type and assorted replaceable blades; possibly half a dozen small artery forceps not larger than the six inch; a couple of longer sponge forceps for cleansing the vaginal vault; one or two cervical tenaculæ; a clip and suture removal set, in these days of early ambulation and short hospital stay; a small six or seven inch needle driver and an assortment of small round and skin cutting needles for minor operative procedures in the office are essential.

There is probably no better method of handling a chronic cystic cervicitis than by radial electrocauterization and there are few conditions so frequently met with which respond so well to treatment. A very useful and relatively inexpensive outfit is put out by National with a basic unit of the transformer with light and cautery outlets. For other minor procedures of cautery and electro-coagulation, I have found that the instrument known as the Hyfrecator is possibly the next most useful. This ingenious instrument is reasonably priced at around $50.00 and performs an amazing number of duties in the office. Lastly amongst the pieces of equipment should be a small sterilizer. There is no need for an elaborate instrument and one can be obtained for around $25.00 or $30.00, that is quite able to do the job. For those of you who may not have access to an autoclave, a pressure cooker on a hot plate is an adequate and satisfactory substitute, which will sterilize gauzes, gloves, sutures, etc., easily and inexpensively. The same principles apply here as in autoclaving.

Probably to your amazement this is about all you need to start the practice of medicine, with the exception, of course, of your hæmoglobinometer, red and white blood counting sets and your microscope, which it is assumed you already have. It is actually a mistake to clutter up one's office with unnecessary instruments, which are seldom ever used and which are expensive to start with.

From the foregoing, it can be seen that the important items necessary in setting up an office for the practice of medicine are not those which are obtained from a medical or surgical supply house. Certain basic instruments are necessary, it is true, and these can be few in number and very basic. Later, when one is established, the addition of

a quartz lamp for helio therapy and a crystal-controlled, Inductotherm type of diathermy machine are probably good investments; particularly the Inductotherm. Used with discretion, this machine will pay its purchase price several times over in the first year or two. Those of you in country practices, later on might well consider the value of installing one of the smaller portable x-ray units, such as the G.E. Model F-4 with floor stand. These units, complete, cost between $1,300 and $1,500 new; used ones can sometimes be obtained for between $700 and $900 with new tubes guaranteed by the factory. A word of caution with respect to the purchase of a diathermy machine. By reason of the sudden imposition by the department of Transport, Radio Division, of restrictions limiting diathermy machines to approved crystal controlled types only, many units were hastily developed with insufficient engineering research, and have proved none too satisfactory in use. The best one available in the writer's opinion, at the time of writing, is the General Electric model D-1.

It is the writer's hope that his experience in these matters by the trial and error method, may help some of you to avoid some of the expensive and unnecessary pitfalls that will beset you early in practice. The old adage that one must crawl before one can walk is equally true here, and if you are not absolutely certain that you need an instrument or a piece of equipment, then do not buy it until you *are* absolutely certain, and even then be cautious. Be content at first to use second-hand equipment, as long as it is in good serviceable condition; remember that you can charge off all invoices under $50.00 as operational expense deductible from income tax, later on when you are actually in practice. That is the time to replace used equipment with new items.

Do not be too hasty in over-subscribing to journals, until you are sure of the ones you want, and do not hesitate to cancel or change a subscription, if you do not feel it is earning its keep. The same applies to medical books. It may not be common knowledge, but a good proportion of new medical books are the brain children of the publishing companies, stoutly though they may deny it, and are usually re-hashes of previous works. The well-established texts and references you know, have stood the test of time, and will stand you in good stead. Beware of highly advertised cumulative loose leaf systems, unless your heredity includes a long line of filing clerks! Nine out of ten gather dust, not new inserts! In addition, they are very expensive in relation to their practical value.

Experience. Remember that on graduation you probably will know more about medical science than you ever will in the future, but you will never know less of the art of it's application in practice—this knowledge comes with experience. Be not backward in cultivating with deference the friendship of the older practitioners in your community, for they can teach you much. In one of Harvey Cushing's addresses occur the following thoughtful words: "It is my hope that with the Lord's Grace, the passing years will endow whatever small knowledge I may possess with that aura of Experience so vital in the Art and Practice of my craft. . . ."

May the writer wish you all, every success in the coming years.

Editors Note: The author, in recommending certain manufacturers' instruments by name, expresses his own opinion; this does not necessarily signify endorsement of these products by the UNIVERSITY OF TORONTO MEDICAL JOURNAL.

THE ELECTRON MICROSCOPE IN MEDICAL RESEARCH

ALICE E. WHITESIDE GRAY, B.Sc., M.D.*

THE UTILITY of the optical microscope has been limited by the nature of light. For over a decade prior to 1932 physicists had considered the possibility of using electrons instead of light in a microscope. The first magnetic electron microscope was constructed in 1932 by two German physicists, Max Knoll and Ernst Ruska. In their instrument they applied two important principles. The first was that electrons moving through a vacuum have associated with them waves of exceedingly short length. Secondly, these electrons can be focussed by magnetic and electrostatic fields, just as light rays can be focussed by a glass lens. The first results were not spectacular, but by 1938 really good pictures were obtained by the German investigators. In 1934 under the direction of the late Professor E. F. Burton of the Department of Physics of the University of Toronto the early experiments were repeated and by 1939 the first instrument on the American continent was constructed at Toronto by Albert Prebus and James Hillier. It was not long until the ungainly research models were replaced by the present day streamlined, compact commercial instruments.

The magnetic electron microscope is the type used most commonly for biological research. In spite of the fact that this instrument differs radically in appearance from the optical microscope there are many analogous features.

In the electron microscope a source of electrons emitted from a heated tungsten filament is substituted for ordinary light. Electromagnetic lenses formed by a coil enclosed in an iron shield with a central ring or air gap are used instead of glass, and the image is not focussed by changing the relative position of the lenses but by alterations in the intensity of the magnetic fields in the electromagnetic lens coil. As complete a vacuum as possible is necessary in the instrument because the electrons would be deflected or stopped by the molecules of oxygen or nitrogen. In the light microscope, the object is seen by transmitted light: in the electron microscope only scattering and diffraction of the electrons by the object play an appreciable role and the degree of scattering increases with the thickness and density. Electrons can not penetrate ordinary glass slides. The objects, therefore, are usually mounted on thin plastic membranes of about 10 millimicrons in thickness. The image is focussed upon a fluorescent screen and a permanent record may easily be recorded on a photographic plate.

The important practical advantages over the optical microscope are due first to the increased resolving power. The degree to which any optical instrument can detect the separation of particles which are extremely close together is called its resolving power. The resolving power of the oil immersion lens of a good optical microscope is 0.1 micron. The practical limit of resolution of the electron microscope is 0.001 micron. Thus in the electron microscope fine particles and fine detail can be photographed. Secondly, greatly increased depth of focus gives useful magnification in three dimensions.

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The different properties of light and electrons make it inevitable that different kinds of preparations are needed for optical and electron microscopy. Methods of preparation of specimens for the electron microscope are still being developed, are often primitive and must be modified for the particular problem involved. The opacity of all matter to electrons necessitating the examination of very thin preparations and the need for exposing the specimen to a vacuum are the most important limitations on the use of the instrument. So far efforts to overcome the latter disadvantage have not been successful. The usual methods of preparation of specimens may be grouped under the following headings, (*a*) suspensions of minute particles, (*b*) thin sections of the material to be examined, (*c*) surface films, (*d*) replicas that reproduce the surface contour of thick objects.

Suspensions of particles are examined after depositing them on a very thin membrane. A modification has been to incorporate them into the membrane but the former procedure has been more useful as a routine. The usual method of preparing a thin film is to dip a glass slide in a 0.1% solution of a plastic, formvar, in ethylene dichloride. On removal the ethylene dichloride evaporates leaving a thin film on both sides of the glass slide. If the film is cut with a needle in squares it may be floated off on water and then supported on a metal grid. The metal grid consists of a woven wire screen having about two hundred meshes to the inch. Suspensions of particles for microscopy can then be placed on the plastic covered grid as small drops. When the drop dries the mount is ready for examination in the microscope. Many modifications of this general method are possible depending on the concentration of the suspension. For example if the suspension is concentrated the excess fluid may be removed; if the suspension is dilute several drops may be allowed to evaporate. Sometimes it is of advantage to let the droplets settle on the grid as an aerosol. Freeze drying of the mount has been useful in dealing with certain materials. It has been found that the fine structure of the film interferes with the visualization of objects smaller than ten millimicrons. Metallic films of extreme thinness which appear uniform under the electron microscope have been prepared but they are extremely fragile.

Since thin sections of animal tissues have proven so useful in the study of cells in the light microscope it has been natural to try to prepare similar sections for the electron microscope. This has been a very difficult problem since much thinner sections are required and hence different methods of fixing and embedding are necessary to preserve intact the finer structure that the electron microscope displays. Satisfactory sections have been obtained for examination in the electron microscope. These have been prepared either by altering the ordinary microtome or by the use of specially developed high speed microtomes. One of the most important factors in the quality of the sections is the edge of the knife used in sectioning. It is obvious that very careful grinding and stropping is imperative. More difficult even than the cutting is the problem of how to preserve undamaged the minute detail the electron microscope can reveal. This involves first methods of fixation. Osmic acid fixation has been used and formalin has had a limited trial. Neither of these fixatives is adequate and experimentation continues. Embedding has usually been carried out in

hard paraffin or collodion plus paraffin mixtures. Ordinary staining procedures cannot be used. When properly prepared sections can be made consistently, comparisons of normal and malignant cells will be possible. Baker in California has had some success in this undertaking. Interpretation of the fine structure heretofore unseen, presents many difficulties.

A preparation coherent and thin enough not to need a supporting membrane is ideal for electron microscopy. These preparations are uncommon but have been obtained from collagen fibres. Naturally occurring fibrous substances such as tobacco mosaic virus protein will develop a skin and thus can be examined directly. Layers of tissue one cell thick have made very interesting preparations. A group under Porter have shown that it is possible to grow cells in tissue culture over grids. Sometimes areas of cells are found thin enough for examination after the necessary dessication. Healthy and diseased cells can thus be directly compared. Porter has shown differences, for example, in the protoplasmic detail of normal and malignant cells. Fixation is again of extreme importance in this as well as in the sectioning technique.

Thick objects may be examined by means of a replica or copy of their surfaces. This technique has been employed with advantage in the study of bacteria. Excellent replicas can be made of the surface of cultures in a Petri dish by flooding them with dilute solution of formvar and draining till dry. The film then readily separates and can be floated ofl and mounted on screens in the usual manner. This may give a true replica of the growth surface or a so-called "pseudo-replica" in which some of the bacteria and products of growth are actually incorporated in the plastic. Similar preparations can be made of smears of cells on glass slides. Positive replicas or replicas of replicas can also be made. High temperatures are involved in this procedure so it is applicable to very few biological problems. Teeth have been examined in the greatest detail and the technique may be altered for such diverse materials as skin, bone, and nail. Again this technique may be modified to meet the particular requirements of the specimen.

Williams and Wyckoff introduced a technique in which heavy atoms of a metal, chromium for example, are deposited on the surface of the specimen. The deposit is made obliquely in an adequate vacuum and as the metal travels in straight lines none is deposited behind the particles. Micrographs of these preparations give the impression that the particles have cast a shadow. The technique was originally devised as a means of determining heights of particles by measuring the lengths of the shadows but the three dimensional quality of the preparations and the increased visibility of small detail have superseded the intended advantage in importance.

Electron micrographs have been made of many objects which themselves are big enough to be seen in the optical microscope; the most important of biological origin and interest are the bacteria. Of the inorganic material the study of metallic dusts, particularly those occurring in mines, has given information on silicosis. Methods devised in this field have been used in the study of mists and fogs in the investigation of atmospheric pollution. The study of cells has already been mentioned. The structure of sperm cells and chromosomes has been investigated with the discovery of new details of internal

organization. Protozoa, yeasts and moulds are too thick for direct examination but micrographs have been made of their processes. The details of the flagellar systems of spirochaetes have been photographed and the presence of an outer membrane confirmed. No clear answer as to the method of multiplication of spirochaetes has been found although the theory of longitudinal fission has received encouragement. In the application of the electron microscope to the study of bacteria much information has accumulated as to the general morphology, and the investigation of the finer structure of the bacterial cell particularly in the illusive search for the bacterial nucleus. It is difficult to correlate structure seen in stained cells with those seen in the necessarily unstained preparations examined in the electron microscope. The study of bacteria undergoing lysis by bacteriophage gives a very important picture of the fine structure of bacterial cells. Differences can be observed depending on the age of the organism, for example there is evidence of a fluid state of the protoplasm in very young cells becoming gel-like as the culture ages. The electron microscope has confirmed the existence of a bacterial membrane as well as the existence of flagella. Sporulation and germination have been observed also. In micrographs of dividing cells transverse separatory membranes have been seen to develop before actual splitting takes place. The rickettsiae have been extensively investigated and micrographs confirm the existence of a capsular membrane as well as suggesting fission as the method of multiplication.

The examination of viruses was one of the most obvious fields of application of the electron microscope. Viruses of all sorts have been studied and the resolution of the instrument is so great there has been no trouble in photographing even the smallest. The identification of the virus from the normal particulate material has proven to be the real problem. Virus purification after release from the infected cell has required great ingenuity and in certain virus diseases where cell death occurs before the concentration of virus is very high the causative agent has eluded photography. The viruses of the pox and psittacosis groups have shown a distinct morphology. The poxes have a brick-like shape while the members of the psittacosis group are spheres. Definite membranes have been demonstrated on all these particles. The influenza virus has been photographed adsorbed on chick red blood cells and certain strains of this virus give evidence of both a rod and filamentous form. Several viruses which are of interest in cancer research have been studied. Spherical particles have been observed in preparations of milk of female mice which are carriers of the so-called milk factor. These may be the viral agent. Studies have been made of spherical bodies from other malignancies and compared to the normal particulates in the tissue involved. Several attempts have been made to photograph the virus of poliomyelitis but its identification is still uncertain. The plant viruses have received considerable attention, particularly the chemically purified virus protein of the tobacco mosaic disease. So far no mammalian virus has been isolated in the form of a crystalline protein. The bacteriophages that are the agents of virus infection of bacteria have proven to be interesting objects of study. Bacteriophages appear to be specific for only a few strains of a bacterium. They have shown variations in morphology as to size, shape of the head and length of tail.

Very comprehensive studies have been made of the growth and multiplication of bacteriophage and in the study of these virus-like entities there is a field of investigation which will contribute much to an understanding of the fundamentals of the living process.

There are many proteins whose molecules are of a size to be photographed. These include certain enzymes and antibodies and even the globulins of human serum. These substances constitute a very fertile field for future research. The electron microscope revealed unsuspected information on the fine structure of the fixed supporting of the fixed supporting tissue of the body. Tendon in particular was given an exhaustive study in the very early history of the electron microscope. The fine structure of muscle as demonstrated by the work of Schmitt, Hall and Jakus is a classical example of the role the microscope may play in an integrated study of a tissue.

The electron microscope is one of the most important new tools in experimental medical science. The manner in which it has extended scientific knowledge has been briefly surveyed with no attempt to list all of the applications but merely to mention a few of the more important areas in which research is being conducted.

D.V.A. BENEFITS

The retiring Ex-Service Representative, H. R. Rowsell has announced that D.V.A. policy regarding educational benefits has not changed. Those who have been granted extension of benefits will be granted further extension, providing the necessary academic standing is maintained. In the Faculty of Medicine, D.V.A. has chosen an arbitrary level, corresponding to second class honours.

The Ex-Service student who fails, and who is still entitled to benefits, can have these benefits reinstated on successful completion of the year missed.

Dual Establishment Allowance benefits will again be granted to those students who must maintain another domicile in a city or town other than the one in which the students who are interning or attending University.

Graduating ex-service students who are still entitled to D.V.A. benefits (either through qualifying time, or through extension) will be granted remuneration on the present basis for a twelve month period of junior internership, upon application. Application may be made in writing, or in person, any time after the publication of examination results. For those students leaving Ontario, application should be made to the D.V.A. Office nearest to the hospital in which the student is interning. It is very doubtful if remuneration will be made to a student interning in the United States. Proof must be given that a suitable Canadian hospital interneship is not available.

Benefits for further post-graduate training may be applied for, but the applicant must have had high honour standing as an undergraduate, and it must be shown that the proposed training will contribute to successful rehabilitation and be in the public interest. Special D.V.A. requirements apply to such post-graduate training, and the individual student should discuss his case with D.V.A. authorities.

BACTERIAL FOOD POISONING

JUANITA E. WOOD, B.A., 5T2

FOR MANY YEARS, it was believed that food poisoning was chiefly due to the presence in food of "toxic amines," or ptomaines, which resulted from protein decomposition. Later, it was shown that these substances were relatively non-toxic, and, moreover, that they did not appear until protein decomposition had reached such an advanced stage that the food was repugnant to the normal senses. The theory of ptomaines was laid aside when it was discovered that most cases of food poisoning were of bacterial origin.

Bacterial food poisoning is now classified into two groups. The *infection* group includes those forms which follow the multiplication, within the body, of pathogenic organisms contained in the food. The *toxin* group includes those forms which follow the ingestion of food in which poisonous substances have been elaborated as the result of bacterial proliferation.

THE INFECTION TYPES OF FOOD POISONING

SALMONELLA FOOD INFECTION

Outbreaks of the Salmonella type of food infection are most commonly due to *S. enteritidis* and *S. typhi-murium*. However, intensive study of the Salmonella group during the past few years has revealed a number of other strains which may be responsible for Salmonella food infection, particularly *S. cholera-suis*, *S. thompson*, and *S. newport*.

The chief modes of conveyance of Salmonella food infection are the consumption of the meat, milk, or eggs of an infected animal, and the pollution of food by human carriers or by infected rats, mice, or other animals. In outbreaks due to food derived from infected animals, *S. enteritidis* or one of its varieties is most frequently found; while in outbreaks due to sound meat contaminated during the course of its preparation as food, *S. typhi-murium* is the predominant organism.

It is possible to differentiate three main clinical forms of Salmonella food infection, the characteristics of which are respectively: (*a*) acute gastro-enteritis, (*b*) typhoidal syndrome, and (*c*) bacteremia. The severity and the nature of the resulting illness are governed by the type of Salmonella involved, but differences in virulence or toxicity among strains of the same type probably cause equally significant variations in the clinical picture. The number of organisms ingested is an important factor. In some experiments as well as in some outbreaks, individuals who have had a small dosage have escaped without symptoms.

The incubation period is 12 - 36 hours, after which there is a sudden onset of nausea, vomiting, abdominal pain and diarrhœa accompanied by fever and prostration. The abdominal pain and diarrhœa are often severe, but the illness is typically over within a few days. An attack may be ushered in with headache and chills. The causal Salmonella is often recoverable from the fæces of patients with characteristic symptoms.

Statistics relating to the incidence of Salmonella food infection are notoriously unreliable. The true incidence of in-

fection has been obscured through the inherent difficulty of isolating Salmonella organisms actually present in the incriminated food or in the fæces of its victims and also "through ascription to Salmonella food poisoning of many outbreaks in which no viable organisms of this group were present." There is, however, some reason to believe that Salmonella food infection may be relatively more prevalent in Great Britain than in North America. According to Hinden, reports from England and Wales over the 15-year period, 1923-1937, showed 299 outbreaks of Salmonella food infection affecting 4,418 persons, of whom 102 died, giving a recorded case fatality rate of 2.3 per cent. Considerable fluctuations from year to year were noted. There are no strictly comparable statistics for North America. Fuchs reports for the United States in 1939, an exceptionally high total of 148 outbreaks of food poisoning of all kinds involving 3,782 persons with 12 deaths. The low case fatality rate probably reflects a relatively low incidence of Salmonella food infection.

Shigella Food Infection (Bacillary Dysentery)

Food-borne Shigella infections are primarily due to the contamination of foodstuffs with the Flexner or Sonne organisms by human carriers or by flies.

The incubation period is usually 1 - 6 days, 48 hours being the average time elapsing before the onset of symptoms. The main features of an attack are diarrhœa, abdominal pain, fever and prostration. Vomiting is less characteristic.

"The fact that consumption of the flesh, milk or eggs of infected animals is not a recognized mode of transmission of bacillary dysentery to man, accounts for the lesser incidence of food-borne infection due to the Shigella group as compared with the Salmonella group. A similar explanation possibly underlies the delayed recognition of food-borne infections due to the Shigella group. The 1919 milk-borne Flexner dysentery epidemic in Aberdeen, reported by Kinloch, which involved 1,000 persons, of whom 72 died, is apparently the first instance of record of a proven Shigella food poisoning outbreak." (Dolman)

Control

The control of the infection types of food poisoning depends in large measure upon raising the level of community sanitation. Everything should be done to prevent the access of rats, mice or other animals to food destined for human consumption. A thorough system of meat inspection is essential. The meat of diseased or emergency-slaughtered animals should be condemned. To this precaution alone, Meyer attributes the comparative infrequency of meat-borne food infections in California where it is known that calves are frequently infected with *S. enteritidis*. Measures should be taken to ensure the cleanliness of premises where prepared foods are made. It is particularly important not to employ cooks who have previously suffered from enteric infections. Every effort should be made to detect carriers and to train food handlers in the methods of cleanliness.

THE TOXIN TYPES OF FOOD POISONING

Staphylococcal Food Poisoning

Certain strains of Staphylococci are enterotoxigenic. The toxin is produced during the multiplication of the organisms in such foods as milk and milk

products, pastries containing custard or cream fillings, ham and potted meats, and many others. In most cases, contamination is due to the handling of food by persons with staphylococcal infections of the skin, naso-pharynx or throat, but air-borne contamination is also possible. Another important factor is the endogenous infection of milk with Staphylococci in cows with mastitis.

The incubation period of staphylococcal food poisoning is 1 - 4 hours. This is followed by a period of nausea which may last for only a few minutes or for an hour. Sudden vomiting then occurs and may be repeated several times over the next few hours. In addition, there may be abdominal cramps and marked diarrhœa. The pulse is rapid, the temperature is often raised, and the patient may be apprehensive or collapsed. After 3 - 5 hours, sometimes sooner, improvement sets in. Often, however, for several days, anorexia may persist with nausea, diarrhœa or abdominal discomfort and a considerable loss of weight. The mortality rate is extremely low, but a few apparently authentic fatalities have been recorded.

Although staphylococcal food poisoning is the commonest of the food poisonings, its actual incidence is unknown. The nature of its syndrome is such that outbreaks are likely to be recorded only when fairly large groups are involved.

Control is by the sanitary handling of food, pasteurization of milk and milk products, and refrigeration of foodstuffs. Staphylococci multiply readily in meats and pastries displayed in shop windows and may be present in enormous numbers in food without changing its appearance, odour, or flavour.

Botulism

The causative agent of botulism is *Cl. botulinum*. Five types, *A*, *B*, *C*, *D*, and *E*, are recognized on the basis of the production of type-specific toxins. Three of these types, *A*, *B*, and *E*, produce toxins which are lethal for man. The potency of pure, crystalline, type *A* botulinus toxin is such that the fatal dose for an adult man, calculated on the basis of experiments with mice, probably contains not more than 0.016 micrograms of nitrogen. Of the three types which have been encountered in human botulism, type *A* is the most common, while type *E* is the least common and the most recently recognized.

Cl. botulinum is widespread in the soil and on fruits and vegetables. Normally, the organism is unable to grow in the animal body and give rise to infection, consequently fresh foods, cooked or uncooked, may be eaten with impunity. For botulism to result, the organisms must multply and form toxin in the food before consumption. The factors which determine the survival, germination, multiplication and toxin production of *Cl. botulinum* in canned foods are: (*a*) the presence of the spores in suitable numbers, (*b*) inadequate processing, (*c*) anaerobic conditions, and (*d*) too slow cooking. Records show that home-canned foods are more dangerous than commercial products.

The incubation period of botulism is generally under 24 hours, although a much longer time may elapse before symptoms become evident. Prominent among these are vomiting, constipation, ocular paresis, thirst, pharyngeal paralysis, the secretion of thick, viscid saliva, and, sometimes, aphonia. The temperature may be normal or subnormal. General consciousness and sensibility remain intact until near death which is preceded by coma or delerium. Usually, death is due to respiratory failure. It

may occur within 24 hours of the onset or it may be delayed for a week. In patients who survive, complete recovery, particularly of ocular movements, may not take place for 6 - 8 months.

There are 6 recorded outbreaks of botulism in Canada, involving 38 persons with 22 fatalities. Although each of the first three of these presented the typical symptomatology of botulism, in none was *Cl. botulinum* isolated. In each of the three subsequent outbreaks, the organism was isolated and twice found to be type *E*. It should be noted that in nearly every instance, the diagnosis of botulism was not made until after the deaths of the patients. It is most important, therefore, to keep this disease in mind when diagnosing every case presenting a syndrome similar to that described above.

In the United States, the incidence is much higher. Meyer has estimated a minimum of 463 outbreaks, involving 1,253 persons with 816 deaths, over the period, 1899-1947. Reports of outbreaks in the British Isles are notably rare.

Nearly all the reported outbreaks of botulism have been caused by food that has been smoked, pickled or canned, allowed to stand for a time, and eaten before cooking, or after inadequate cooking. Usually, the food is abnormal in appearance and odour. Bulging of the tin, the presence of gas bubbles upon opening, a disintegrated appearance, or a rancid odour should be sufficient to condemn the canned food. On no account should such food be eaten even after cooking. Unfortunately, in some cases, spoiling is not evident. It is of the utmost importance, therefore, that every precaution be taken during home-canning. The hands of the person preparing the food should be well washed and the food thoroughly cleaned. Only reliable canning and processing equipment should be used and the instructions should be followed rigorously.

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A PROBLEM IN DIAGNOSIS

T. A. McLENNAN, 5T0

PRESENTATION OF CASE

P.B., A THIRTY TWO YEAR OLD white housewife was admitted to the Emergency Department of the Toronto General Hospital on December 20, 1949. She complained of lower abdominal pain of twelve hours duration.

This patient had been in excellent health until 1945. At that time she suffered an attack of severe, steady, lower abdominal pain that persisted for twenty-four hours. This episode occurred six weeks following the delivery of her third child and no other symptoms presented.

Twelve weeks before admission she gave birth to her fourth child. Intercourse was attempted two weeks later but was not completed because of dyspareunia. Four weeks after this she experienced another attack of lower abdominal pain that was accompanied by a yellowish vaginal discharge. Streaks of blood in the urine were noticed about this time but there were no urinary symptoms. Six weeks before admission she went to bed feeling weak and ill. Within a few days an aching soreness had developed in her left loin and lower abdomen. A diagnosis of urinary infection was made by her doctor and she was treated by bed rest and Sulfadiazine. This was continued until arrival at hospital without apparent effect.

On December 20, 1949, the morning of admission, she awoke with extreme lower abdominal pain that was more marked on the left. This pain required constant sedation for relief. She was unable to eat, but did not feel nauseated.

The patient's menstrual life began at fourteen years of age and has been regular—consisting of a twenty eight day cycle with a moderate flow lasting seven days and unaccompanied by pain. Her last menstrual period began on October 31, 1949 and lasted seven days. This bleeding, beginning one month after delivery and two months before her present admission, resembled a normal period.

Until the present time the patient had been pregnant four times and had delivered four normal children, aged twelve years, nine years, four years, and three months respectively. There were no complications during pregnancy or at delivery. No other significant, relevant history was obtained.

Examination on admission showed a pale, thin girl of thirty-two years who perspired freely and appeared acutely and severely ill. The oral temperature was 103 degrees F., pulse rate was 130 per minute, blood pressure was 100/60 and the respiratory rate was 20 per minute.

Significant physical findings were limited to the chest and abdomen. The heart appeared slightly enlarged to percussion and a loud, blowing systolic murmur was heard in the pulmonary area. The abdomen was not distended but was exquisitely tender and rigid in both lower quadrants. Rebound tenderness and pain on movement or coughing were referred to the left lower quadrant. A firm, tender mass was palpated arising out of the pelvis, and reaching half way to the umbilicus, on the left side. The liver and spleen were not palpable and no costovertebral tenderness was elicited.

On vaginal examination the cervix was soft, mobile and pointed down and back. Inspection showed cervical oedema and a normal, parous, undilated os.

On bimanual examination the fundus of the uterus was anteverted and to the right. It was firm, somewhat tender and appeared fixed to a fluctuant, tender mass, the size of a grapefruit, in the left fornix. This was continuous with the abdominal swelling and seemed distinct from the uterus. Rectal and recto-vaginal examinations revealed an uninvolved rectum.

Laboratory examination showed a trace of albumin and ketones in the urine, a haemoglobin of 81%, a white blood count of 14,700, a Westergren sedimentation rate of 80 mm. in one hour, and a negative blood Wassermann. The non protein nitrogen was 28 mg.% and carbon dioxide combining power 53.8 volumes %.

Following pelvic examination, the patient went into shock with a blood pressure of 70/40, a pulse rate of 130 per minute, and a rectal temperature of 104 degrees F. Treatment during the next twenty four hours consisted of sedation, intravenous fluids, blood transfusion, Penicillin and Streptomycin without improvement. Immediate operation was deemed necessary. Bimanual examination under anaesthesia confirmed the clinical findings and posterior colpotomy was negative for blood and pus.

DIFFERENTIAL DIAGNOSIS

Because of the history, physical examination and laboratory findings it is possible to exclude such conditions as *pyelitis*, *appendicitis* and *diverticulitis*.

Ectopic pregnancy with tubal rupture is suggested by a six week period of amenorrhoea, sudden severe lower abdominal pain more marked on the left side and accompanied by shock, and a palpable mass in the region of the left adnexa. Against this is the history of a previous attack, a relatively high temperature in company with shock, a low white blood count for recent severe bleeding, a high sedimentation rate, the absence of nausea, vomiting, vaginal bleeding, and a posterior colpotomy negative for blood and pus. Haemoglobin determinations are of little value in the presence of dehydration as hemoconcentration may occur even with recent severe bleeding. The Aschheim-Zondek test is of value if previously positive, if it is done immediately, or if it is found to be positive. The finding of decidual elements without the presence of chorionic villi is characteristic of the vaginal bleeding in this condition.

Ovarian cysts may present similar pelvic findings without symptoms. The sedimentation rate is not elevated unless infection occurs and then the picture becomes that of acute pelvic inflammatory disease with an encapsulated pelvic abscess. These cysts may attain a large size, can be bilateral, usually are fixed and frequently are tender. Acquired dysmenorrhea may be produced by those cysts due to endometriosis and prolonged, profuse, irregular bleeding commonly occurs. A properly done posterior colpotomy makes a diagnosis of ruptured ovarian cyst unlikely. Sudden shock with signs of peritoneal irritation is rarely due to a ruptured vessel in the pedicle of an ovarian cyst undergoing torsion.

Infection of a *degenerating fibroid* cannot be ruled out but a history of amenorrhea makes it unlikely.

Pelvic Inflammatory disease is the favoured diagnosis. Gonorrhoea is the leading cause of such inflammation but a history of exposure may be difficult to

obtain. Discharge is usually due to cervical irritation. A minority of cases are due to B. coli and Streptococci following post-abortal, puerperal or peri-appendicular infection. Tuberculosis is uncommon without a primary focus elsewhere and Actinomycosis does not find this area a site of choice. In all these conditions the fever is usually of moderate degree, the white blood count is between 12,000 and 20,000, the sedimentation rate is elevated, and vomiting and chills are rare. Bilateral salpingitis occurs by extension from below and tends to set up a localized pelvic peritonitis and peri-appendicitis; hence severe, bilateral, lower abdominal pain is characteristic. Some degree of bilateral, tubo-ovarian abscess formation is the common and unfortunate sequel to untreated or inadequately treated cases. The Gonococcus is usually absent from the tubes two to four weeks after the fever disappears and hence cultures taken at operation are likely to be negative. In view of the first attack occurring six weeks post partum and the absence of a history of neisserian exposure or attempted abortion this is likely a puerperal infection.

CLINICAL DIAGNOSIS

Tubo-ovarian abscess

TREATMENT AND CLINICAL COURSE

On laparotomy, December 21, 1949, a large abscess about 10 cms. in diameter was found adherent to the posterior surface of the left broad ligament and to the left side of the uterus. It involved the ovary and the tube on that side. Generalized pelvic inflammation with pelvic peritonitis and peri-appendicitis was present. Bilateral salpingo-oophorectomy, subtotal hysterectomy, and appendectomy were carried out. The post operative course was uneventful and the patient discharged thirteen days later.

PATHOLOGICAL REPORT

The cystic mass from the left tubo-ovarian area measured 10 x 8 cm. and was smooth and shiny. On cutting into the mass the wall was seen to be cystic and about 2 mm. thick. The internal surface was rough, shaggy and partially filled with a soft, light yellow, purulent material. Microscopic examination showed this to be an old corpus luteum cyst that had become an abscess cavity. Bilateral peri-salpingitis, right sided peri-oophoritis and peri-appendicitis was present. The abscess cavity grew B. coli and streptococci.

FINAL DIAGNOSIS

Ovarian abscess

SUMMARY BY DR. H. B. VAN WYCK

The chief point of interest in this patient was the problem of diagnosis. The history suggested some type of post partum sepsis. The palpable pelvic findings were unlike those of salpingo-ovaritis, a pelvic cellulitis, or a pelvic abscess, in as much as there was a round well defined cystic mass fairly movable and so closely attached to the uterus that it was difficult to determine that the whole mass was not merely an enlarged uterus without the passage of a uterine sound. Posterior colpotomy failed to reach the pus cavity. The pre-operative possibilities were, an infected degenerating fibroid or ovarian or par-ovarian cyst. It proved to be an intra-ovarian abscess developing in a corpus luteum with coincident bilateral peri-salpingo-ovaritis.

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EDITORIALS

WHAT HAVE THE FIVE YEARS MEANT?

A few of the questions on the JOURNAL'S final year questionnaire were purposely made thought provoking. Only 39 of the 89 answering took the bait, but what they wrote is interesting.

"The romance is gone" was the predominating note. Medical men no longer have "the god-like wisdom and super-human attributes" once accorded them. Perhaps this is only growing up, but there were numerous complaints about susceptibility to pecuniary motives, strife and envy, coldness and petty-mindedness. One bitter spirit called the whole profession "a fraudulent hoax." To some it was disquieting to know that diagnosis is so often uncertain, that there is so much left unknown in medicine. A few are left with a sensation of helplessness, rather than power. Others feel that no other profession has done so well for mankind; one, that it is man's only hope.

To most there has been a change in the value placed on human life. Some have seen it increase, others decrease, and both processes often occurred in the same person. Personal responsibility for life had brought to many the knowledge that every life is valuable, especially one's own patients. The series of wonder drugs leads some to feel that no life should be despaired of. At any time some new cure may be found for a previously hopeless condition.

Most had noted an increasing tolerance for their fellow men, and believed they were less critical. A few described their readjustment perhaps too bluntly, stating that their moral standards had fallen during the course. "I have adopted Horace's Golden Rule, moderation in all things. (But I am not just drifting with the current)," states another.

Some few had derived a new meaning and conviction in religion during the course of medicine. Others had wrapped themselves still deeper in the dark cloak of agnosticism. There was no openly stated grudge against God, as might have been expected after the first world war. Those interested in the Kingdom of God were thinking on the level of personnel work rather than general policy.

There was little material forthcoming on what medicine had done to the mind. Most who answered felt they had been broadened, and that their power to reason was enhanced. "I can accept nothing unless it has a rational background." All of which suggests that the drug salesman of the future should be argumentative rather than dazzling.

One man would have preferred engineering, wanting an outdoor life. Another would like to have been in business administration. The other 87 are happy with medicine, feeling there is no more worthwhile activity.

In assessing the above it will be realized that most are minority opinions. However it is safe to assume that where one man speaks, he is not alone but represents a number of less self-conscious and self-confident people. Most of the replies denied that medicine had changed their opinions or beliefs. Perhaps this is because most of us change our minds like we change our skins, by an imperceptible process of growth and exfoliation. It is only the odd man who puts off a complete skin like a snake or a dragonfly and is the more self-conscious because of it. Everyone of us has been changed by five years between the anvil of the examinations and the hammer of the Faculty.

D. J. L.

THANK YOU!

In this, the last number of Volume XXVII of the JOURNAL, we wish to express our appreciation to those who, in various ways, have made possible these six issues.

First, we thank all the students, members of the Faculty, and alumni who have contributed to these pages or in other ways have taken an interest in the JOURNAL.

To the Managing Editor and the Circulation and Advertising Managers we are particularly indebted for their efficient handling of the business of the JOURNAL. Through their efforts, previous circulation and advertising records have been broken and the JOURNAL has had a financially successful year.

The Associate and Assistant Editors and the Abstracts and Features Editors did much to lessen the work of the Editor-in-Chief by capably executing their duties; they and all the other members of the staff helped in many ways.

Special thanks are due to our Consulting Editor, Dr. W. G. B. Casselman —his experience and willing co-operation helped us to circumvent many technical and editorial pitfalls; to Mr. J. Weir and other members of the staff of the University of Toronto Press who once again have taken a personal interest in the JOURNAL; to Mr. C. Hart for the many services he has done for us, and to Mr. E. F. Peacock of the University of Toronto Alumni Association for helping to re-introduce the JOURNAL to many former readers. Lastly, we extend our thanks to our subscribers and advertisers for their loyal support.

Next year the JOURNAL will be edited by Mr. D. E. Yates; knowing his capabilities, we are confident that volume XXVIII will be better than ever.

FEATURES

MEDICAL RESEARCH AT THE UNIVERSITY OF TORONTO, PART II

G. CHERTKOW, B.A., 5T0
M. L. A. AUERBACK, 5T2

IN THE FIRST ARTICLE of this series, the general nature of medical research at this University was outlined, and many of the projects were discussed. This article will survey, briefly, those research projects being undertaken which have a more immediate clinical application. Unfortunately, many projects must be omitted due to space limitation.

Throughout most of this research, an attempt has been made to correlate closely laboratory research and clinical studies. Research is used to arrive at a satisfactory explanation of common clinical problems and enable adequate diagnosis and treatment to be made. Thus most of this medical research impresses the observer as being of a highly practical nature.

CARDIOVASCULAR RESEARCH

One significant project is a long term critical evaluation of the present methods of treating cardiac failure. One of the big problems in such analyses has been the establishment of proper controls. Toronto workers have tried to overcome this by establishing a standard method of treating cardiac patients. The clinical examination includes history, physical examination, weight records, and estimation of vital capacity. The usual treatment for such cases includes a 1 Gm. salt diet, a program of bed rest, the use of Digitalis Leaf, and weekly or bi-weekly diuretics. The average period for recovery from failure is about twelve days, and this is followed by a three week period of bed rest. Having established this standard method of treatment, workers in Toronto are now trying to determine the comparative value of other methods of treatment such as a decreased period of bed rest, Digitoxin tablets, the use of various types of diuretics, or diets with various amounts of salt. These alterations are substituted in the routine treatment. It is proposed to treat alternate patients with the routine treatment or the experimental method. In this way, a significant control series can be set up, and the effects of the suggested variations can be properly evaluated.

Toronto workers are also trying to establish a method of differentiating early cardiac and early pulmonary dyspnoea through measurements of the vital capacity, and its subdivisions. Changes in the functional residual air, which forms one fraction of the vital capacity, are being observed over an experimental period during such manipulations as postural changes, drug injections, etc. It is felt that these changes may be significant in differentiating the early forms of dyspnoea and enabling more accurate diagnosis of early cardiac failure to be made.

Congenital malformations are a prominent cause of early cardiac disease. Many of these can be successfully treated but the patients first require extensive investigation. A series of studies is now being made to demonstrate these con-

genital defects. One technique currently being employed is cardiac catheterization whereby tubes are passed into the heart, so that the oxygen content and blood pressures in the various chambers can be recorded. A second method used in this study is angiocardiography in which X-ray photographs are taken as an opaque material passes through the heart. By these studies, it is usually possible to demonstrate which congenital defects may be aided by operation.

Cardiac surgery is now receiving considerable attention in a number of research centres. Some of the fundamental problems in this type of surgery form the basis of several significant projects at Toronto.

One group of workers is investigating general hypothermia as an anaesthetic and also as a method of reducing the body oxygen requirements sufficiently to allow the exclusion of the heart from the circulation. This would permit intracardiac surgery under direct vision. The fundamental physiology and biochemistry of general hypothermia has been studied in dogs, and methods have been developed for reducing their body temperatures with relative safety to 20°C. and to a minimum of 14°C. with survival. At 20°C. the oxygen consumption, cardiac output, blood pressure, and heart rate are about 15% of normal. Thirteen dogs have had exclusion of their hearts from circulation for 15 minutes, with later return to normal body temperature. In 6 of these, the heart was opened and resutured. This procedure is still attended by a high mortality rate. A study of the cause and control of death has been a major aspect of this research. Rewarming of the animals has been studied by immersion in water at 40°C. and by the use of short wave diathermy.

Another group is experimenting with the extracorporal circulation in dogs in an attempt to produce a relatively bloodless field in intracardiac surgery. The procedure has been to occlude the venae cavae at their entrance to the heart and deliver oxygenated blood at normal blood pressure into the aorta. This blood, entering the aorta in the opposite to normal direction, closes the aortic valves and floods the coronary circulation. Various artificial mechanisms have been used to oxygenate the blood, but the lung of the dog sacrificed has proven the best oxygenator to date. The right auricle and right ventricle have been opened into and explored on numerous occasions. It is hoped that this method of obtaining a bloodless field will be applicable to intracardiac surgery in humans since, during the operation, the patient would be on a temporary heart-lung system better than his own.

Another group has devised a technique of observing the living vascular bed through a microscope. The occurrence of intravascular agglutination or "sludging" of blood has been studied in many forms of injury, including shock, in anaesthetized animals. Experiments are in progress to determine whether these circulating clumps of cells may be partly responsible for the blockage of circulation in the kidney in unexplained cases of anuria, such as the "crush syndrome" or traumatic anuria. Also, a search is being made for a substance which will deagglutinate these clumps.

The determinations of the amount of oxygen in the blood is of considerable value, as in the procedure of cardiac catheterization, in cardiac operations and in cardiac diseases. Yet the methods now available require too much time. Therefore, a group is trying to

perfect a rapid determination of blood oxygen by the use of a photoelectric colorimeter, based on the changes in the optical density of blood produced by combination of oxygen and haemoglobin. It is hoped to obtain an accurate and simplified method. Another group is studying the changes in arterial blood saturation with oxygen produced in chronic pulmonary disease, under conditions of rest, exercise, breathing oxygen, etc.

MALIGNANT DISEASE

One problem in treating cancer of the cervix today is to select the radioresistant or radiosensitive lesions so as to determine if treatment by surgery or radiation is most desirable in each case.

A major study is being made to determine the effects of radiation on stage I and II cancer of the cervix, by means of observing changes in the normal and malignant cellular elements of the vaginal smears. It is hoped that eventually one could predict the response to radiotherapy and select the early radioresistant cases which might be better treated by surgery. Vaginal aspirations and surface scrapings are used and stained by the Papanicolaou method.

Another interesting study is being made to determine the true incidence of *carcinoma in situ* or intra-epithelial carcinoma of the cervix, by means of routine serial sections on all cervices, including normal ones, that are removed surgically. This may clarify the status of *carcinoma in situ* in the development of carcinoma of the cervix.

Folic acid antagonists are substances similar to folic acid in structure, which have been suggested as possible aids in the treatment of acute leukemia. At Toronto, an appraisal of their values is now being made. They appear to give temporary remission in one third of cases.

PHARMACOLOGICAL RESEARCH

A number of workers at Toronto are investigating some of the newer anaesthetics with a view to evaluating their efficiency and toxicity. Currently, they are studying the cardiac irregularities caused by anaesthesia. This same group is also examining the new narcotics that are appearing on the market in order that their identity can be established in medico-legal cases.

Antabuse, a drug that has recently received a great deal of publicity, is now being tested by researchers on both animals and humans.

A chemical similar to thyroxine that may effectively antagonize this hormone in cases of hyperthyroidism, is also being studied.

An interesting project now in progress is the investigation of the clinical possibilities of Trilene. At Toronto, it is being used as an obstetrical analgesic in the first stage of labour, and as an anaesthetic in the second stage. It may prove of considerable value to the general practitioner for the relief of pain in labour.

HEPATIC RESEARCH

There is still much that is unknown about the disturbance of liver metabolism in various acute and chronic hepatic diseases. An intensive study is now being made to correlate the course and clinical findings of these diseases with the results of laboratory determinations and liver function tests. The study includes determinations of serum proteins, amino acids, urea and blood cholesterol,

liver function tests, studies on the development and control of ascites, and evaluations of changes in carbohydrate metabolism and diuresis. It is hoped that these studies will aid in the diagnosis and effective treatment of liver diseases.

Other workers have observed the varied pathological picture found in the livers of babies that die of severe infections, such as intestinal intoxication.

They are trying to correlate the clinical course and dietary histories of these babies with the postmortem liver findings. They are also investigating the influence of lipotropic substances on the state of the liver in babies with severe intestinal intoxication.

For several years, investigators at Toronto have been preparing a liver extract of extremely high purity for use in the treatment of pernicious anemia. From this they have separated crystals which appear to be identical with the newly described vitamin B12. The value of B12 in treating pernicious anemia is now being studied.

RENAL RESEARCH

Several laboratory tests have formerly been used in renal diseases to differentiate disturbances in glomerular filtration from deranged tubular function. The validity of these differential tests is now being investigated. Also, the comparative value of low and high protein diets in renal disease is being determined by noting the effects of protein intake on animals with experimental anuria.

HEMATOLOGY

An interesting study is being made of the Rh blood factor. Rh negative females are being screened out of large groups in the population and their blood is tested for the presence of Rh antibodies. Their children are also being investigated. The methods of treating Rh incompatibility, by simple or replacement transfusions, are being appraised. Particular attention is being paid to the comparative value of male and female blood in transfusing infants suffering from incompatibility. The experimental effects of the Rh hapten which may remove Rh antibodies present in the maternal circulation, are being studied.

Other investigators are studying an abnormal blood globulin fraction which appears to develop in certain infections, liver diseases and other conditions. It is precipitated by 13% sodium sulfite, unlike other globulin fractions which are precipitated by greater concentrations. They have also developed methods of examining serum to distinguish considerable dilutions of an abnormal haemoglobin derivative called methaemalbumin. This occurs in some of the rare spleen-liver syndromes. These abnormal blood proteins may aid in problems of differential diagnosis.

NEUROLOGICAL AND PSYCHIATRIC RESEARCH

A five year follow-up study is being made of patients subjected to prefontal leucotomy. This study includes electroencephalography before and after operation, personal interviews and estimation of changes in social, emotional and intellectual functioning. E E G records are also being studied for their relationship to personality traits, psychomotor epilepsy, and the prognosis in depressions treated by electroconvulsive therapy.

Amongst other projects, investigations are being made of the metabolic, endo-

crinological, and psychological aspects of anorexia nervosa. The long term results, and the degree of recovery in treated cases of meningitis are also being studied.

Poliomyelitis is the subject of an extensive study. The aim is to increase our understanding of the disease, its mode of spread, and its occurrence in both paralytic and "minor" forms. The behaviour of polio is being studied over several years in a stable, rural population from clinical, epidemiological, and laboratory aspects. Experimental animal research has been aimed at the development of a simple test for the detection of the polio virus.

SPECIAL SENSES

Eye research includes a program concerned with the prevention of blindness from glaucoma, and studies into the use of orbital implants in sockets after enucleation, in order to improve the motility of artificial eyes. Toxoplasmosis, familial eye diseases, and the treatment of orbital socket infections are being studied.

An acoustic laboratory is in operation to study deafness. New methods of testing hearing loss in children are being attempted, with the examiner not being seen by the patient. These acoustic studies are being correlated with the rehabilitation of deaf veterans and the assessment of their hearing loss. The endosteal regeneration of bone is also being studied to determine why early closure of the opening occurs after fenestration operations.

NUTRITIONAL AND DIGESTIVE RESEARCH

There is a considerable amount of research being conducted at this University in the field of nutrition. One of the many projects deals with the nutritional value of finely ground, cooked bone. This has been added to commercial meat preparations as a source of calcium and protein. Rat growth studies have been made, to see if the protein of bone is high grade. These appear to indicate that bone protein mixed into meat in a 10% mixture may not decrease the biological value of meat, and may be of value.

Studies are being made of digestion, especially to determine what disturbances occur in coeliac disease and fibrocystic disease of the pancreas. The duodenal contents and post-mortem pancreas have been examined for their enzyme contents, and the level of intestinal phosphatase determined. Attempts have been made experimentally to reproduce coeliac disease, and fibrosis of the pancreas with zinc compounds. Studies have been made of accurate methods of diagnosing these and of the effects of such therapy as the administration of vitamin B-complex and saponifiers.

ENDOCRINOLOGY

Toronto investigators are studying the effects of various conditions, such as malnutrition, and the administration of exogenous dessicated thyroid by mouth, on thyroid function. Thyroid function is estimated by clinical studies, BMR, and changes in the levels of serum protein precipitable iodine. Determination of the level of this iodine is made by a colorimetric method which has proved to be an accurate indicator of thyroid function.

A new steroid laboratory has recently been established. Here, research has been initiated in the methods of isolating and determining steroid hormones, their

effects on isolated enzyme systems, and the excretion of these hormones in certain diseases, such as cirrhosis, endometriosis, schizophrenia, threatened abortion, and adrenal disorders. The steroids include the 17-ketosteroids, the adrenal corticosteroids, pregnandiol, and oestrogens.

INFECTIOUS DISEASES

Tuberculosis is being studied at Toronto from several different aspects. One survey is concerned with the incidence of endobronchial tuberculosis in children, which may be more common than formerly supposed. Studies of the effects of streptomycin, sulphones, and certain salicylic acid preparations on tuberculosis, are being undertaken to determine their efficiency and adequate dosage.

B.C.G. vaccine is also being investigated, especially in regard to the method of preparing and distributing it in a stable, dry form. At the same time, other workers are studying the ability of acid-fast and Gram negative organisms to produce antibiotic substances which might be effective against the tubercle bacillus or Gram negative organisms.

METABOLIC DISEASES

A variety of studies are being conducted on all aspects of diabetes mellitus. One project is an extensive detection survey which is studying representative samples of the population in order to determine the true incidence of diabetes. This will aid in the detection of unknown diabetics and the assessment of the magnitude of the problem in Canada.

Workers in Toronto are also studying the high incidence of degenerative changes which occur in the eyes, arteries, kidneys, and hearts of patients who have had diabetes for over fifteen years. These people, in spite of their youth, have accelerated "aging processes." Experimental studies are being carried on with diabetic animals to see if similar changes occur in them, to assess the value of dietary factors, and to prevent the early degenerative changes. These studies may also aid in understanding the aging processes which normally occur in later life.

The electrolytic upsets in diabetic acidosis, ketosis, and coma are being studied. Special attention is being given to changes in the potassium and inorganic phosphate levels because of their possible relationships to proper therapy in these conditions.

Studies are also being made of toxaemia, a metabolic disorder occurring in pregnancy.

GASTRO-INTESTINAL RESEARCH

Long-term and follow-up studies are being made of clinical cases of regional ileitis and ulcerative colitis. One group is attempting to reproduce ulcerative colitis in dogs. There, the effects of un-neutralized pancreatic ferments, especially trypsin, are noted on normal animals, on those with damaged colons, and on those whose colons have been damaged by lysozyme.

Other investigators are trying to find the cause of death in intestinal obstruction which goes on to strangulation. They have isolated experimentally a closed segment of bowel which retains its mesenteric attachment. Death usually occurs in four days, through swelling and perforation of the bowel, with peritonitis. The injection of penicillin, streptomycin, sulfadiazine, and

other substances into the bowel, however, has prolonged life up to twenty days. These interesting observations are being followed up.

CONCLUSION

Modern medicine is a dynamic science which depends for its progress upon the work being done in many research centres throughout the world. These centres are the fountains from which the Profession draws its strength and wisdom. Let them dry up, and medicine becomes static and dogmatic.

We have endeavoured to describe some of the investigations being carried on at the University of Toronto. From this focus of medical research flows a stream of knowledge from which investigators throughout the world select the information they require to further their own studies. As we mentioned before, much of the work done at Toronto cannot be classified as sensational; nevertheless, it is important because it is research of a practical and fundamental nature that often provides the foundation for medical advances made in other centres.

If the University of Toronto is to continue to be an integral part of international research, however, the ranks of her workers must be continually augmented by imaginative and ambitious young students who possess those certain qualities that mark the true scientist. We have tried to indicate, in these articles, the many opportunities that await these students who relish the challenges that only medical research can present.

ACKNOWLEDGMENTS

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THE CLASS OF 5T0

In keeping with a recently established Journal custom, we present the results of a poll conducted among the members of the class of 5T0. Although only 56% of the year responded, we feel that the opinions expressed in the 86 questionaires that were returned present a fair picture of the graduating class.

In table 1 certain features of this and the three previous graduating classes are compared. A significant change this year is the increase in the number of ex-service students. This in turn probably accounts for two other significant changes: the decrease in the number of women students, and the increase in the number of married men. Most of the bachelors plan to marry later, after internship, while a few plan to take the plunge prior to graduation.

TABLE I

	5T0	4T9	4T8	4T7
Total	158	156	130	130
Men	95%	84%	84%	88%
Women	5%	16%	16%	12%
Married	39%	18%	....	9%
Ex-service	81%	15%	....	....
Navy	16%	40%	....	....
Army	30%	10%	....	....
RCAF	53%	50%	....	....
CWAC	1%	....	....	....

It is scarcely surprising that a class composed mainly of veterans should have a higher average age than previous, non-veteran years. The average student in 5T0 is 26, about three years older than his counterpart in the three previous graduating classes. The comparative distribution of ages is given in table II.

TABLE II

Age in years	5T0		4T9	4T8	4T7
21	..		4%	1%	5%
22	2%		35%	44%	29%
23	6%		24%	32%	26%
24	17%		11%	10%	24%
25	18%		8%	4%	7%
26	19%		2%	2%	5%
27	12%				
28	15%	46%	16%	2%	4%
29	9%				
30 and over	10%				

When not busy in the classroom, 30% of the students took part in various interfaculty athletics, of which basketball, rugby, soccer, swimming, and hockey were the favourites. The others enjoyed their hobbies of outdoor activities, music, literature, and photography. In the evening, the students read the Daily Star, Time, Life, and the Saturday Evening Post. With their breakfast coffee, most preferred the Globe and Mail.

When asked to express their views about socialized medicine, 80% declared themselves opposed to it. An equally great percentage, however, felt that it would come to Canada in some form or other. This did not appear to worry them particularly, since only 10% stated that they had altered their career plans to meet this eventuality. It is interesting that a number of those expressing opposition to the concept of socialized medicine suggested that some form of health insurance was needed in Canada.

Eighty per cent of the class of 5T0 stated that they enjoyed university life. Those who did not gave as the main reason the great amount of work that they had to do in the course. Others felt that their responsibilities at home prevented them from enjoying the various university activities. "I would have enjoyed college life if I had been 10 years younger," a number remarked.

After graduation, 42% plan to intern for one year, 43% for two, while a few will intern for from three to five years. The future plans of this and the three preceeding graduating years is indicated in table III.

TABLE III

	5T0	4T9	4T8	4T7
Undecided	16.0%	4%	17.0%	14.4%
General Practice	54.0%	57%	27.0%	28.0%
Specialty	26.0%	40%	56.0%	58.0%
Specialty after general practice	1.0%	4%		
Specialties:				
Surgery	8.0%	8%	20.0%	10.0%
Paediatrics	3.5%	3%	8.0%	10.0%
Undecided	3.5%	11%		
Internal Medicine	2.3%	5%	12.0%	10.0%
Obstetrics	1.1%	2%	20.0%	13.0%
Psychiatry	1.1%	6%	10.0%	5.0%
Neuro-psychiatry	1.1%			
Neurology	1.1%		.8%	1.6%
Radiology	1.1%		.8%	1.6%
Ophthalmology	1.1%	5%	.8%	1.6%
Physical Medicine	1.1%			
Anaesthesia	1.1%		.8%	1.6%
Military Medicine	2.0%			
Medical Research	1.0%	2%		

The class of 5T0, apparently, will contribute twice as many general practitioners as the classes of '47 and '48. Inasmuch as the students this year are older than their counterparts of a few years ago, this should not be unexpected.

The information derived from that part of the questionnaire devoted entirely to the ex-service students proved to be quite interesting. Seventy-five per cent of the veterans completed high school prior to enlistment; the remainder reached their junior matriculation. Not all planned to go into medicine; indeed, one third had such careers as engineering, teaching, accountancy, optometry, and theology in mind. Fortunately for the Faculty of Medicine, they changed their minds while in the service, or at discharge when the plans of DVA became known. Forty per cent feel now that they would never have gone to Varsity if it had not been for DVA. DVA supported 60% for the entire course, 30% for from three to five years, and the remainder for less time. All but two veterans expressed deep gratitude to the government for this help. "It was the best thing that ever happened to me," several stated. Almost all agree that if they had the choice again, they would still take medicine.

Thus we see that the average student of the class of 5T0 differs to some extent from his predecessors of earlier days. He is older, more mature, and saddled with more responsibilities (10% of the class have children). He will not take as much postgraduate training, but will, instead, become a general practitioner after a year or two of internship. Unperturbed by the thought of socialized medicine coming to Canada, despite his dislike for it, he does not expect to alter his plans because of it. His home life and abundant hobbies will more than fill any time that his work leaves free as he slowly progresses towards his goal of becoming the oldest practising medical practitioner in Canada. M.L.A.A.

HUMANISM AND MEDICINE

H. B. VAN WYCK[1]

PART XII

THE 16th CENTURY REVIVAL OF THE DIRECT STUDY OF NATURE

With the recovery of the ancient classical literature, scholars first directed their attention to classical philosophy, history and poetry, and thus the revival of interest in the so-called humanities came before the revival of interest in science. Those who were interested in the works of literary merit had seldom sufficient scientific knowledge to understand the works of science, just as the men of science seldom had sufficient knowledge of the ancient languages to read the old records. It would appear that the progress of science depended more on the order of the printing of these ancient works than on the discovery of the old manuscript texts. Among the earliest scientific works to be printed were the *Natural History of Pliny*, 1469, and editions of Varro in 1471. The medical works of Celsus appeared from the press in 1478. These were all in Latin and not until 1476 was actual Greek type used. The scholar-printer Aldo printed the first Greek editions of Galen and Hippocrates in 1526, following which scores of editions in both Greek and Latin appeared and were very widely studied.

Rebirth of a faith in the appeal to nature had appeared in the works of Roger Bacon, but this new element in late mediaeval thought fell into the background after Bacon's death in the 13th century. It reappeared in the 15th century in the works of the Rhinelander, Nicolas of Cusa (1401-1464). This lofty philosophic genius recorded a careful experiment on a growing plant and proved that it absorbed something of weight from the air—the first biological experiment of modern times. Nicolas Cusanus showed that he understood the experimental method and undoubtedly many of his suggested investigations were a stimulus to Galileo a century and a half later. Another pioneer was Leonardo da Vinci (1452-1519), who stands at the turning of the Renaissance towards modern times. This universal genius, artist and scientist covered the whole field of mathematics to physiology, and his anatomical and embrological studies were not surpassed for several centuries.

Another embodiment of the new spirit was the Swiss genius known as Paracelsus (1483-1541). This boastful and garrulous teacher at his first lecture at Basel performed the symbolic act of burning the works both of Galen and of the Arab, Avicenna. Paracelsus did share the forward-looking programme of Francis Bacon; he did wish to see the world in the light of nature; and though his methods were violent and often incoherent and repellent, he played his part in the transmission of a new attitude towards the investigation of nature. There was no lack of contemporary

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genius. The great painters began to study nature with greater accuracy. Verrocchio (1435-1499), Botticelli (1444-1510), and the great German, Albrecht Dürer of Nuremberg made painstaking reproductions of details of human anatomy. Dürer had as catholic an outlook as Leonardo and conducted experiments in optics, perspective, and mathematical properties of sound. Remarkable works on botany appeared with reproductions of great truth and beauty. The most remarkable of these early botanists was Leonard Fuchs (1501-1566); and the same type of interest, applied to the animal body, culminated in the works of the real father of modern anatomy, Andreas Vesalius (1514-1564). A Belgian, from the Universities of Louvain and Paris, Vesalius was finally appointed professor of anatomy at Padua in 1537, when he began his radical reforms. Vesalius first did away with the demonstrators and other intermediators between himself—the teacher, and the object—the body being dissected. At the age of 28 he produced the *De Fabrica Corporis Humani* printed at Basel in 1543, the first great modern work of science and the basis of modern biology. His drawings, whether by himself or others, are of a very high standard. It is true, however, that Vesalius still venerated Galen and he, therefore, held the physiological view of Galen which depends on the supposed existence of pores in the intraventricular septum. That he was mystified can be seen as he writes:

"The septum is formed from the very densest substance of the heart. It abounds on both sides with pits; of these, none, so far as the senses can perceive, penetrate from the right to the left ventricle. We wonder at the art of the Creator, which causes blood to pass from right to left ventricle through invisible pores."

In the second edition of his great thesis, however, he writes:

"The septum of the heart is as thick, dense and compact as the rest of the heart. I do not see, therefore, how even the smallest particle can be transferred from the right to the left ventricle through the septum."

This marks the point of inception of a scientific revolution. No longer is tradition enough and Vesalius was the first among many Italian anatomists who ultimately influenced the great awakening of biological investigation in the 17th century.

It was obvious that the observations of Vesalius, with his passion for accurate detail, threw into pitiless relief the errors of the Graeco-Roman Galen, and the new *De Fabrica* caused a tremendous sensation in the universities of Europe. Here was an anatomist who had gone to the human body for his facts. His teacher, Silvius, turned against Vesalius, and heaped upon him ridicule and abuse. It was safer to run full tilt at established authority with Paracelsus at Basel than it was in Italy where prejudice was strongly entrenched and supported by a reactionary church. It was dangerous to advance new ideas especially about the body which was of interest to certain minds only because it housed the soul. Indeed, as far north as Geneva in 1553, Servetus was burned at the stake by a religious despot outside the old church, John Calvin. Servetus had anticipated Harvey to some extent by pointing out the importance of the pulmonary circulation and how the blood, being mixed with air, returned to the heart. Like all his predecessors, because he had no microscope, he missed the capillary junction between arteries and veins. He made a shrewd guess, however, and paid for his daring with his life. Likewise Vaselius found all the great of Padua,

indeed, of Italy, turning against him, for no other reason than that he tried to tell the truth as he saw it. Vesalius resigned his professorship, burned his notes, and went to live in Spain where he died in 1564. It was dangerous in the 16th century to question established dogmata about the body.

It was much safer to investigate the stars. By the 16th century, astronomy began to lose its mediaeval or Ptolemaic character. This was perhaps due to the publication of the works of Regiomontanus who wrote on trigonometry and completed a digest of the astronomy of Ptolemy. Leonardo da Vinci, about 1510, explained the reflected light on the moon. Fracastor (1483-1543) added to our knowledge of astronomical theory and practice, especially with reference to comets. Overshadowing all these was the great Nicolaus Copernicus, the Pole (1473-1543). Copernicus had a broad course of study in several Italian universities in both the humanities, theology, law and the sciences, including medicine. From his study of mathematics, Copernicus was led to seek a new theory of the heavenly bodies. His scheme retained much of ancient theory. It still assumed that the universe was a sphere and finite, and that the orbit of celestial bodies is always circular. To ascribe these new movements to the earth, as Copernicus did, in his *Revolution of the Heavenly Bodies*, was to run full tilt into well-established prejudice. For more than a thousand years Ptolemy had reigned. The geocentric theory of the universe died hard and Copernicus was opposed by Luther and Bacon as well as by hosts of lesser and more ignorant people. To these in a strange preface to his work, Copernicus sounded a note of freedom and defiance:

> "If perchance there shall be idle talkers who, though they are ignorant of all mathematical science nevertheless assume the right to pass judgment in these things, and if they should dare to criticize and attack this theory of mine because of some passage of scripture which they have falsely distorted for their own purpose, I care not at all. I will even despise their judgment as foolish."

Three years after the death of Copernicus, the Dane, Tycho Brahe was born. This patient and accurate observer was the darling of the occupant of the Danish throne, and on the island of Huen in Denmark, the largest and most elaborate observatory in the world was built for Tycho. Here he spent twenty years making observations and correcting the data afterwards published as the Rudolphine tables. Although Tycho did not sense the truths of the geocentric element in the Copernican theory, his observations created modern astronomy and were the foundations upon which Kepler and Newton built. His description of the perturbations in the moon's motion had to await explanation by subsequent generations. He first observed that the movement of a comet may not be circular and his numerous calculations of the planets enabled Kepler ultimately to reveal their true orbits.

Less striking than these advances in scientific knowledge were the changes in the practice of medicine and surgery of the day. The profession of medicine in spite of its auspicious beginning in the Hippocratic age, had remained, in the absence of more accurate knowledge of physiology and the other ancillary sciences, a profession which was dominated by authority and vitiated by much superstition. It was a matter of an undue reliance on bleeding, purging and the uncritical use of a well-stocked, but uncertain pharmacopeia. Surgery, how-

ever, was in a worse plight during the middle ages because, while medicine was in the hands of the priestly order who were comparatively educated, the practice of surgery had been abandoned to an illiterate class of barbers, bone setters and primitive physiotherapists. These barbers, whose hands performed most of the surgery until the 15th century, were a class of outcasts. Why surgery had been completely abandoned by the clergy and had been degraded to a low level, is difficult to explain. One among many other explanations, each of which may have a bearing on the problem is that the practice of medicine was a clerical rite, and that a canon of the church prohibited physicians from drawing blood on pain of excommunication. Hence surgery, avoided by the priests, fell into the hands of the vulgar who practised it without direction, knowledge or conformation to a standard. These barber surgeons were itinerant in many cases; moving to a district, they exploited it before moving to another. Certain families became specialists in certain operations, such as those for cataract, calculus, or hernia, and transmitted their secret routines to their posterity. Such conditions prevented effectively the development of the profession of surgery. However, with the disappearance of the prejudice against dissection in the 13th century, a few of the clergy dared to perform surgical operations and this tendency increased during the 14th and 15th centuries until we find in the 16th that the great anatomists of that period, such as Benivieni, Vesalius, Fallopius, and Fabricius were all skilful and popular surgeons.

The two professions came together by a significant event which happened in France in 1515. A small brotherhood of St. Côme, an organization of surgeons, had found themselves contending against the Faculty of Medicine on the one hand and the barber surgeons on the other. They sought a way out of their difficulty by asking and obtaining recognition from the university. This event marked a Renaissance of surgery, not only for Paris, but for the whole world. By this reunion the faculty acquired authority over the barber surgeons and thus surgery and medicine became united.

Surgery, however, now made faster progress han medicine, and among those who contributed to its advance in the 16th century is the name of Ambroise Paré. Born in 1510 at Laval, of poor parents, he was apprenticed at an early age to the provincial barber surgeons. He studied three years at Hôtel Dieu in Paris, and at this time gained the confidence of the staff. It is probable that in Hôtel Dieu he was acting as a sort of house surgeon, doing dressings, performing venesections, and assisting at postmortem examinations. It is unlikely that he had regular clinical instruction.

In 1537, Paré became a military surgeon appointed to the army which King Francis I was assembling in Provence to repulse the Emperor Charles V. At this time it was orthodox surgical treatment to pour boiling oil into every amputation, or indeed in other wounds in order to stop haemorrhage. Paré narrates the experience of his first campaign, an experience which led to one of his great innovations. In the aftermath of the skirmish in the Pass of Susa, the boiling oil gave out, and yet Paré noted that those who were treated with it did not do as well as those who failed to obtain it. This led Paré, who recounts all this in his *Book of Arquebus Wounds*, and in his great *Apology*, to state that the orthodox treatment was wrong. A

characteristic comment of Paré appears several times as a coda to his clinical histories as follows:

"I treated him and God cured him."

This has a modern ring although it recalls as well the great statements of Hippocrates about the *Vis Medicatrix Naturae.*

In 1552 at the siege of Damvilliers, Paré amputated a leg and for the first time omitted the use of the cautery, using in its stead ligatures to the veins and arteries. The patient, grateful to have escaped the agony of the cautery, made a good recovery. In 1554, this brilliant career was signalized by Paré becoming without examination master of the College of St. Côme. In 1559 he became one of the surgeons of the King of France, a position he held during the reigns of Henry II, Francis II, Charles IX, and Henry III. A contemporary wit was led to remark that the Kings of France transferred to their successors their court surgeon as a legacy of the Crown. It was universally conceded that Paré's extraordinary services as surgeon to the army were responsible for enabling the city of Metz to survive the siege laid to it by the armies of Charles V. After this, the brotherhood of surgeons of St. Côme admitted Paré to an examination in spite of the fact that he lacked the qualification of a knowledge of Latin, and in the face of bitter opposition from the members of the faculty of the University of Paris. Paré had an extraordinary and successful career. From the excitement of military camps, he would pass to the large civil practice which grew rapidly with his fame. He was an omnivorous reader and wrote himself a great number of works on surgery and, contrary as it was to the custom of his time, he was eager to make his views, results, and discoveries known to all.

"For my part I have dispensed liberally to everybody the gifts that God has conferred upon me, and I am none the worse for it; just as the light of a candle will not diminish no matter how many may come to light their torches by it."

Not only did Paré become expert in surgery but he advanced the art of obstetrics, restoring to the practice of his day the forgotten technique of podalic version, a very useful procedure when indicated, especially before the days when Caesarean section had become reasonably safe. Paré died in 1590.

All these advances aroused a general interest in the new scientific method, and this was reflected in the growth of the universities. At first the Italian universities held the first rank, but soon these were superseded by the French, and finally the German universities rose to pre-eminence. The new learning attracted enormous numbers of students; thousands thronged to Boulogne and Naples. At the University of Wittenberg in 1520 there were about 600 students; in Erfurt, 300; and Leipsic had 400, while about the same time there were 7,000 students in the University of Vienna. Teachers and students migrated from place to place and faculties were constantly changing. The students often chose the Rector and officers of the universities, and sometimes assisted in determining the structure of the curriculum. In some Scotch universities at present the students continue to elect the Rector.

The students were divided into bodies called "nations" according to country. These had special seals and were the parents of the later student-corps in German universities. Certain representatives were chosen from each of these "nations" and constituted a College of Rectors. These negotiated with of-

ficials of the state and acquired great power which they retained until the end of the 16th century. The poorer class of students went from one school to another, supporting themselves by singing, begging, or stealing, and were oftentimes guilty of great lawlessness. Although many of these travelling scholars fell into dissolute and vicious ways, some ultimately attained rank and eminence. The students with better financial background tended to proceed south to the Italian universities.

Toward the end of the century the social and mental status of the medical students improved and they began to take their part in the increasing intellectual activity of their age. The spirit of exploration and discovery was abroad. Columbus had enlarged the known world; Copernicus had thrown back the limits of the universe; and the new biology had discovered the wonders hidden in the living organism. The faith and devotion of millions of Europeans had been rudely uprooted by the revolutionary changes in religious belief. Men sought a new faith and the new knowledge promised a boundless world free of darkness and fear. Hope, achievement, adventure, and enterprise became the watchwords of the age, and a voice appeared to sound a clarion call to its spirit of high endeavour. It was Francis Bacon, called by some "The most powerful mind of modern times," who "rang the bell that called the wits together." He made himself the sponsor of the hope and resolve of post-Renaissance Europe. Born in 1561 in London, he lived through the eigns of Elizabeth, James I, and died in 1626. At the age of 16 he was appointed to the staff of the Ambassador to France, following which he had an active life in politics, occupying high offices, until at the age of 57 he became Lord Chancellor. Step by step with his ascent to political power Bacon had been climbing to the summits of philosophy. He aspired to be both philosopher and statesman, and seemed to his contemporaries to realize the Platonic ideal of the philosopher-king. The stimulus of his influence on modern thought is incalculable, and if he did not enter the promised land of science, he stood at its margin and pointed toward its widening vistas of achievement. Bacon has described the quality of his own mind and the strength of his aspirations:

"I found that I was fitted for nothing as well as for the study of truth. As having a mind nimble and versatile enough to catch the resemblances of things (which is the chief point), and at the same time steady enough to fix and distinguish their subtler differences, as being gifted by nature with desire to seek, patience to doubt, fondness to meditate, slowness to assert, readiness to consider, carefulness to dispose, and set in order, and as being a man that neither affects what is new nor admits what is old, and that hates every kind of imposture."

His greatest work was the establishment by energetic and eloquent writings of an understanding of the new method of science which renounced authority and relied upon observation and experimentation. His greatest performance was the *Novum Organum* (New Method). Its text was that "knowledge is power." By the scientific method Bacon taught that one could by achieving a perfect science, achieve a perfect social order. This he describes in his last fragmentary publication *The New Atlantis*. In this he has depicted a society in which at last science has its proper place as the master of things. That this immoderate confidence in natural science as the solution of human ills has n our day been weakened, in no way detracts from the fact that Bacon was a tremendous

intellectual force for centuries. He was the mouthpiece of the century in which he died. In 1662 the founders of the Royal Society of England, the most eminent of scientific societies, hailed Bacon as their inspiration. When the French Encyclopaedists of the 18th century undertook the *Encyclopédie* they dedicated it to Francis Bacon. As he viewed the world merely as an atomic structure ready to be moulded by scientific man, he has been the basis for many a materialistic system of philosophy, and his prophecy of the "fruits" and "commodities" which mankind would produce for itself found formulation in 19th century utilitarianism—the greatest good to the greatest number. To the free spirits of the 16th century no thought occurred that before three centuries had passed an atomic age would have brought despair, disillusionment and the abandonment of all hope in a purely scientific Utopia.

The new optimism that followed the Renaissance may be better understood by a description of the philosophic, religious and political changes that followed the disintegration of the mediaeval synthesis. This description in which it is difficult, perhaps impossible to remain objective will next be attempted.

MEDICAL STUDENTS ON VARSITY TEAMS

The faculty has been particularly well represented this year on Varsity teams. A. J. Cecutti, J. R. Evans, R. D. Longmore, and J. F. Mustard played Senior Varsity Football; J. K. C. Murray, W. E. Noonan, and G. D. Shay played for the Intermediate Varsity team. In Soccer, Medicine was repreented by R. O. Antoni, and E. S. Thompson on the Varsity Senior team; and by R. Wilson on the Varsity Intermediate team. C. P. Vernon played Senior Varsity Hockey; and H. A. Hyde was a member of the Intermediate Varsity Hockey team. The Varsity Senior Intercollegiate Swimming team included E. D. Hubbard, L. Y. Rosen, D. R. J. Smith, and W. C. Trusler; while W. J. Hanham, D. H. H. MacKenzie, and J. R. MacKenzie were members of the Varsity Intermediate Swimming team. The Varsity Senior Intercollegiate Water Polo team included L. Y. Rosen and P. S. Rosen; the Varsity Junior Water Polo team included W. A. Baker, E. D. Hubbard, D. H. H. MacKenzie, J. R. MacKenzie, E. A. Silverstein, D. R. J. Smith, and W. C. Trusler. E. D. Wigle played Senior Varsity Basketball; D. I. R. Dalgleish, H. Coopersmith, W. M. Wilson played for the Varsity Junior Basketball team. C. D. Anderson was a member of the Varsity Intercollegiate Squash team; P. D. Hopkins was a member of the Varsity Intercollegiate Wrestling team; and J. B. Murphy coached the Varsity Intercollegiate Gym team.

The Medical Athletic Association has made extensive plans for its annual Spring Athletic Dance which is to be held Monday, March 20, at the Club Embassy. At this function, Special Athletic Awards will be presented to R. F. Hetherington, Meds 5T0; W. L. Anderson, E. J. Beaton, A. J. Cecutti, K. A. Firman, J. B. McIlraith, Meds 5T1; H. J. Moher, E. S. Thompson, Meds 5T2; M. Lindzon, J. F. Mustard, E. M. Tanz, Meds 5T3. Medical "M" 's are to be presented to G. I. Bernstein, Meds 5T0; H. C. Harley, W. R. Lyon, L. Shack, A. H. Silverberg, J. J. Zeldin, Meds 5T1; J. E. Brunton, J. G. Evans, H. J. Greenberg, J. R. Hilliard, K. W. Hobson, J. E. Knapp, Meds 5T2; J. W. Dawson, T. A. Doran, D. E. Gamble, R. D. Longmore, J. W. McGillivray, J. K. C. Murray, R. L. Ruderman, H. A. Stein, I. Stern, Meds 5T3; R. J. Baird, E. P. Edmonds, H. C. Kilty, D. H. H. MacKenzie, J. R. MacKenzie, R. S. McMillin, R. L. Perkin, L. Y. Rosen, S. D. Sims, D. R. F. Smith, W. C. Trusler, C. P. Vernon, W. R. Walters, Meds 5T4.

ABSTRACTS

MEDICINE

Causes of Melena, H. L. Thompson, D. W. McGuffin, J.A.M.A., **141**: 1208-1213 (Dec., 1949).

This article is a study of 293 cases in which melena was a prominent symptom. Melena was broadly defined to include the discharge of black, red or occult blood from the anus. The site of bleeding and the underlying pathology formed the scope of this study.

Peptic ulcer with its main site in the duodenum was the cause in 29.7% of cases. Melena was the initial symptom in 62% of these cases. Melena from oesophageal varices formed 9.2% of the series. The primary pathological condition was portal cirrhosis in all but two cases where thrombosis of the splenic vein and Banti's disease were responsible. Other oesophageal lesions, including carcinoma and polyp, were to blame in 0.9%. Carcinoma of the stomach was the cause of melena in 7.8% and in 91.5% of these cases, it was massive. Hiatus hernia accounted for 1.7% and acute alcoholism for 1.4%. Sarcoma of the stomach and atrophic gastritis were responsible for 0.6%.

Diverticulitis, duodenal polyp and non-specific enteritis were the cause in 2% of this series.

Diseases of the colon and rectum formed the preponderance of cases in this series. Bacillary dysentery was the cause in 21.5% with most of the cases occurring in the first decade of life. Carcinoma of the recto-sigmoid accounted for 6.1%. Idiopathic ulcerative colitis contributed 5.5%. Colitis secondary to uræmia and non-specific colitis were to blame in 3.4%. Diverticulitis formed 3.8% of the series. Intussusception, 1.4%; polyposis of the recto-sigmoid, 1% and anal stricture, 0.3% formed the balance of the lesions of the colon.

The remaining 0.9% of the series included carcinoma of the pancreas, carcinoma of the prostrate and splenomegaly.

H. R. Rowsell

Use of Para-aminobenzoic Acid in Dermatomyositis and Scleroderma, C. J. D. Zarafonetis, A. C. Curtis and A. E. Gulick, Arch. Int. Med., **85**: 27-43 (Jan., 1950).

The authors had observed that para-aminobenzoic acid (P.A.B.A.) had been used beneficially in disseminated lupus erythematosus. The rationale behind this treatment was as follows: exposure to sunlight may cause an exacerbation of lupus erythematosus; persons receiving sulpha compounds are occasionally sensitive to sunlight; since P.A.B.A. is a recognized sulphonamide antagonist, it was thought that the drug might help persons with disseminated lupus.

Since scleroderma and perhaps dermatomyositis are thought to belong to the same family of diseases as disseminated lupus, the collagen diseases, the authors decided to try P.A.B.A. in the treatment of these conditions.

Six cases are presented. These cases before treatment were mildly febrile and had the constricting, indurated skin lesions of scleroderma, while two of them belonged to the dermatomyositis group with wasting, weakness and lymphocytic infiltration of certain muscles. All showed considerable weight loss.

All six cases showed very definite improvement, and while one died of an unassociated malady, the other five had retained their improvement at the time the paper was written.

It is to be recalled that these diseases are subject to spontaneous remissions and that experience with only six cases, regardless of the excellent results, is inconclusive evidence. However the authors feel that in view of their results further investigation is warranted.

S. H. Witzel

Hypertension Due to Partial Renovascular Occlusion, P. M. Cornwell, New England J. Med., **241**: 1006-7 (Dec., 1949).

Since Goldblatt's experimental production of hypertension in dogs in 1934, many clinical studies have shown that arterial hypertension can result from any type of renal disease that produces a marked reduction, but not complete ablation, of the blood flow through the kidney.

The author reports a case which is unusual in that the pathological process exactly reproduced the conditions of Goldblatt's experiments and it was possible to follow the clinical course of the disease almost from its onset.

This case of hypertension was due to partial occlusion of the right renal artery and the entire development of the hypertensive syndrome was correlated with the clinical symptoms produced

by the arterial occlusion. Cure by nephrectomy and an eighteen month follow-up revealed no tendency to a recurrence of hypertension.

A. Bernstein

Periarteritis Nodosa, S. P. Klein, Archives of Internal Medicine, **84**: 983-1001 (Dec., 1949).

The ætiology of periarteritis nodosa is believed to be a non-specific hypersensitivity reaction to many agents. The pathology consists of multiple focal inflammatory and necrotic changes in the vessel walls followed by a replacement fibrosis and intimal thickening. Thrombi and aneurysms may develop.

The clinical picture varies but symptoms similar to an acute infectious illness are frequently present, *i.e.* malaise, anorexia, pyrexia. An elevated white count and tachycardia are common. At variable times, weakness, muscular and/or abdominal pain and tenderness, and subcutaneous nodules may appear. Cases of acutely swollen and tender joints are reported.

The subcutaneous nodules are usually about 1 - 2 cms. in diameter, circumscribed, indurated, pink, and mildly to non-tender. Diagnosis can be made by biopsy.

The author notes that the disease is not invariably fatal. Treatment is symptomatic and supportive. The average duration of life following the onset of symptoms is under one year. Exacerbations and remissions are frequent.

A. J. Hudson

PAEDIATRICS

Treatment of Erythroblastosis Fetalis by Exchange Transfusion, A. S. Wiener, Postgrad. Med., **7**: 1-10 (Jan., 1950).

The author summarizes his experience in the treatment of erythroblastosis foetalis by replacement transfusion. He explains the significance of bivalent Rh antibodies (agglutinins) and univalent antibodies (blocking antibodies). The degree of erythroblastosis cannot be accurately predicted from the maternal antibody titre since blocking antibodies depend for their action on the presence of complement in the foetal blood stream. As a general rule, however, high maternal titres mean a severe degree of erythroblastosis.

Early replacement transfusion is the method of choice in saving lives and preventing neurological sequelæ. Simple transfusions may counteract the hæmolytic anæmia but are obviously incapable of preventing the intravascular clotting which the author believes is responsible for subsequent physical and mental defects.

A statistical analysis showed a significantly higher mortality amongst infants delivered by caesarean section. The author suggests that in cases in which premature delivery is attempted in order to get a living child, medical induction be used rather than caesarean section.

D. I. Gove

PHYSIOLOGY

The Mechanical Heart-Lung System, J. Jongbloed, Surg. Gynec. & Obst., **89**: 684-693 (Dec., 1949).

The mechanical heart-lung system built by Jongbloed permits the maintenance of complete circulation except that venous blood does not enter the heart and pulmonary circulation. The cavities of the heart are empty of blood or nearly so. Thus this type of heart replaces the organic heart temporarily and does not impose a very short time limit on operation.

Early experiments were done with dogs and it was found that the electrocardiogram of the heart empty of blood was almost unchanged and that the heart and lungs resumed their normal functions immediately upon stopping the mechanical device and removing the clamps, even though these organs had been empty of blood (except for coronary and bronchial circulation) for more than an hour.

In a second series, venous blood was pumped out by two catheters, one through the external jugular vein into the superior vena cava close to the heart and another high in the inferior vena cava through the femoral vein. A second pump forced oxygenated blood into the femoral arteries. A dog treated by this method a year ago is still alive and appears normal. It had lived without using its own heart and lungs for two hours.

The details of the pumping system, spiral oxygenator and regulating system are discussed in some detail. The author believes that the capacity of the apparatus is sufficient for future use in operations on man.

A. Eisen

PSYCHIATRY

Authors and Psychopaths, W. Russell Brain, Brit. M. J., Dec. 24th, 1949, 1427-1432.

Russell Brain explores the relationship of literary genius to mental instability. It is easier

to appreciate the personality of an author than any other type of artist, and we readily see in him writ large the same processes which occur in less gifted patients.

Brain's list of psychopathic authors practically decimates literature. The metaphysical poet, John Donne, was so obsessed with death that he reminded Charles I (later to die on the scaffold), in a public sermon that he "must be mingled with the dust of every highway and dunghill and swallowed in every puddle and pond." Donne indulged his death fascination to the extent of having his portrait painted swathed in a winding sheet, and kept ever before him until he died.

Dean Swift seems to have been incarcerated in the anal phase all his life. The evidence is the fierce misanthropy and the apparent coprophilia of the fourth book of *Gulliver's Travels* He died in an Irish lunatic asylum after several years of restraint.

Doctor Samuel Johnson and his biographer, Boswell, were both troubled mentally. Johnson had obsessive-compulsive tendencies with a horror for death and solitude which led him to seek any company rather than his own and made him a famous but intolerant conversationalist. "Bozzy" was a cyclothyme, with a positive family history. A brother and a daughter were certified for this complaint. His mood swings made him one moment an amiable buffoon and the next a red-eyed determined debauchee, and yet somehow a great author.

Dickens was another manic-depressive, but with marked sado-masochistic trends, shown in the taking of the Bastille in a *Tale of Two Cities*, the murder of Nancy by Bill Sykes, and the more persistent cruelty of Dotheboys Hall. In later life Dickens was able to cash in heavily on his personality by giving readings of his own works. The author acted out all the parts himself and he imparted "to the murder scene such a sense of horror that the audience were semi-paralyzed and sat with blanched faces in absolute silence."

Perhaps the madness and the masterpiece are alike symptoms of the tremendous inward strain. We must not forget that Addison, who gave his name to two diseases, lost a lifelong battle with the manic depressive psychosis and committed suicide in a depressed phase.

D. J. Lewis

SURGERY

Pulp Space Infection and Osteomyelitis of the Terminal Phalanx, H. Bolton, et al., J. Bone & Joint Surg., **31**: 499-504 (Nov., 1949).

The Staphylococcus aureus is most often responsible for pulp space infection. In only a half of the cases is there a history of injury, the portal of entry in the remainder being unknown.

Fibrous trabeculæ at first limit the spread of abscess formation. Spread may occur through these septa, through the periosteum into the terminal phalanx or anteriorly through the skin. The skin and periosteum have the least resistance to increasing tensions and necrotoxins and by the time the septa give way, a sinus to the skin or osteomyelitis has developed. Hardman in 1937 insisted that "the case must be treated before the onset of fluctuation for at this stage the phalanx is dead."

The authors are dissatisfied with the conventional lateral incision used to drain the abscess and attribute "minor causalgia" in 2% of cases to injury to the digital nerve by this method. They recommend an eliptical excision of skin overlying the abscess and the abscess traced down if necessary to the periosteum. The abscess cavity is cleared, filled with penicillin in lactose powder and dressed. Drainage is unnecessary.

A. J. Hudson

Metastasizing Cerebellar Tumors—the Difficulty in Distinguishing Between Medulloblastoma and Neuroblastoma, R. P. Borden and F. H. Lewey, J. Neurosurg., **6**: 439-449 (Nov., 1949).

The authors present three cases of cerebellar tumors in people over twelve years of age. All three were diagnosed medulloblastoma clinically and histologically and received surgical and radiological treatment. Later they developed metastases and biopsy from these sites showed them to be neuroblastomata.

The authors have several suggestions to make regarding this situation:

(1) That the medulloblastoma in people over twelve years of age is different from that in the younger age group in that it is less malignant and can metastasize beyond the central nervous system.

(2) That the cerebellar tumor is in reality a neuroblastoma and a secondary manifestation of a primary elsewhere.

(3) That the patients have had two tumors of somewhat similar histology. This is not very likely.

The authors conclude that these tumors were probably neuroblastomata. They suggest that patients with clinical evidence of a cerebellar tumor, particularly those in the second and third decades, be subjected to X-ray of the chest, skeleton and urinary tract to determine the presence of metastases or of an occult primary tumor outside the central nervous system.

M. FIER

Anesthetic Problems in Cardiac Surgery in Children, W. O. McQuiston, Anesthesiology, **10**: 590-600 (Sept., 1949).

Cardiac surgery has been developed to the point where it can be used in the treatment of various congenital cardiac defects. It may be employed in cases of patent ductus arteriosus, tetralogy of Fallot and coarctation of the aorta.

Preoperative medication was morphine and atropine or morphine and scopolamine. Even infants tolerate morphine very well. This medication depresses them sufficiently so that they are drowsy on reaching the operating room. Frequently cyanosis is lessened following the preoperative medication.

At the Children's Memorial Hospital, cyclopropane has been used as the principal agent in all cardiac surgery even in the presence of arrhythmias. It is administered by the to-and-fro absorption technique with controlled respiration. Generally endotracheal intubation is practised.

Since anoxia is a very serious problem in these children, an attempt has been made to reduce their metabolic requirements and therefore their oxygen requirements. This is accomplished by chilling the child with ice-bags until the rectal temperature is 96 degrees F. With this procedure, very little cyclopropane is required for maintenance of the anæsthetic.

Operative complications encountered were hypoxia, cough, laryngeal œdema and cardiac arrest. Post-operative complications included cerebral anoxia, pneumonia, atelectasis, pleural effusion, hæmothorax and pneumothorax.

In 142 operations there were 19 deaths—a mortality of 13.4%. The causes of death were anoxia, cerebral hæmorrhage or thrombosis, pneumonia, right heart failure, sepsis secondary to an infected cut-down, ruptured pulmonary artery, thrombosis at anastomotic site, embolectomy and empyema.

M. FIER

Experiences with Cardiac Arrest, F. H. Lahey and E. R. Ruzicha, Surgery, Obstetrics and Gynecology, **90**: 108-118 (Jan., 1950).

While the actual incidence of cardiac arrest during anæsthesia is undetermined, the average busy operating room suite may expect 1 - 2 cases per year.

The various ætiological factors are sensitization of the myocardium by chloroform, cyclopropane, ethyl chloride and hypoxia to epinephrine, carotid sinus and vagal stimulation and other less well recognized factors. Diagnosis is established by the disappearance of the pulse and blood pressure.

To prevent permanent cerebral damage active treatment must be instituted within $3\frac{1}{2}$ minutes. To avoid panic it is necessary to have a definite plan of action and the required equipment immediately available. Artificial respiration with 100% oxygen is continued throughout the entire treatment, intubation being advisable to assure a clear airway. Intravenous injection of a mixture of 0.25 cc. of 1: 1000 epinephrine and 5 cc. of 1% procaine is used since some cases of "cardiac arrest" are only apparent and this will often revive a forceful beat. If this fails to give an immediate response, cardiac massage is instituted at once by the transperitoneal subdiaphragmatic, transperitoneal, transdiaphragmatic or transthoracic route, the last being through the fourth left interspace. Massage must be forceful yet gentle and is carried out at approximately one-half the normal cardiac rate. The surgeon must pause occasionally to see if the heart resumes activity. If it fails to do so in a few minutes, 0.25 cc. of 1: 1000 adrenalin and 5 cc. of procaine 1% are injected into the right auricle and massage resumed.

About one-third of all patients so treated will recover completely. A few will die in the next few days because of cerebral damage. Should ventricular fibrillation occur during resuscitation it is best treated by topical or intraventricular procaine.

In addition to a review of the literature the authors present thirteen cases so treated in the Lahey Clinic during the past seven years.

S. H. WITZEL

NEWS AND NOTES

Medical Society

On Monday, March 6, Medical Society Elections were held in the Hart House Theatre. The successful candidates include G. S. Cameron, President; S. L. Wax, Vice-President; J. F. Mustard, Treasurer; W. T. Shaw, Secretary. The president of the permanent executive of 5T0 is D. M. Young. The new Class Presidents are K. E. Roach, 5T1; J. E. Knapp, 5T2; B. Berman, 5T3; G. C. Knupp, 5T4; K. M. Irwin, 5T5. The President of the Medical Women's Undergraduate Association is Miss E. F. Line; the President of the Medical Athletic Association is R. A. Haliburton; the Chairman of Toronto Camsi is B. H. Buchanan.

* * *

On March 2, the Medical Women's Undergraduate Association held its final meeting of this school year. At the meeting gifts were presented to the women of the graduating year. Doctors in attendance at the informal discussion which followed included Dr. E. C. Blatchford, Dr. J. C. Gray, Dr. F. S. McConney, Dr. F. H. Stewart, and Dr. A. T. White.

On March 21, the Medical Women's Athletic Association is holding its annual banquet. At this time University "T" 's, and Medical "M" 's will be presented. Those receiving "M" 's include Miss M. O. Zawadsky, Meds 5T0; Miss R. E. Allison, Mrs. H. L. Reesor, Miss E. M. Setterington, and Miss J. S. Sutton, Meds 5T1; Miss I. C. Hain, Meds 5T2. A pre-medical bar will be presented to Miss S. A. Sarles.

* * *

The year has been an active one for the Medical Men's Athletic Association. Medicine is, at present, fourth in the T. A. Reed Trophy Standing.

* * *

The Editors of the first edition of the Medical Year Book, have announced that copies will be ready for distribution shortly after the end of March. A limited number of extra copies will be available for those who have not yet placed orders. Orders should be placed as soon as possible with some member of the Medical Society Executive.

* * *

On February 22, at the Banting Institute, the Medical Arts and Letters Club heard a highly entertaining and thoroughly informative address from Dr. H. B. Van Wyck on "Music as a Doctor's Hobby". On March 15, the Club enjoyed hearing Dr. W. Boyd reading a programme of selected prose and poetry.

On March 26, the Arts and Letters Club is sponsoring an evening of folk music which will be presented by undergraduate musicians.

* * *

The Student's Administrative Council of the University has accepted $128 from the Medical Society, to establish a fund for furnishings for the proposed University Students' Union. The $128 is the profit realized from the Medical Society sponsored All-Varsity dance, Panacea.

Camsi

The Medical Society has ratified, for the University of Toronto, the motion made at the last annual Camsi Conference, that Camsi should affiliate with the British Medical Students' Association.

* * *

The appointment of Mr. A. L. Halpern, Meds 5T2, as Associate Editor of the Camsi Journal has been announced.

The April edition of the Camsi Journal is being put out by, and is devoted to, the University of Montreal and the University of Toronto.

Faculty

The unveiling of a bronze plaque in memory of the late Dr. C. L. Starr took place in the Faculty Council Room on Thursday, February 16. Dr. Starr was Professor of Surgery in the University of Toronto from 1921 to 1928. The plaque, the work of Mr. Cleve Horne, was presented to the University by a group of Dr. Starr's friends.

* * *

Dr. Elliott P. Joslin, Clinical Professor of Medicine, Harvard Medical School, visited the University on February 17.

Dr. F. H. Bently, Professor of Surgery, University of Durham, Newcastle-upon-Tyne, will be a visitor to the School during the week of March 27.

* * *

An initial grant of $8,200 from the Ontario Department of Health federal funds has

established a research project for the investigation of glaucoma which is expected to take from three to five years to complete.

* * *

Occupational and Physical Therapy have amalgamated to form a diploma course under the direction of the Faculty of Medicine. The new course will be a three year course with no compulsory interning during summer months.

ALUMNI

A Medical Alumni Association Scholarship has been awarded to Mr. G. Y. Hiraki, Meds 5T3.

* * *

The Medical Alumni Association is planning to present the permanent executive of each graduating class with a suitable University of Toronto shield, to be used at all future class functions.

* * *

A refresher course in General Medicine, is being held at the Sunnybrook Hospital, Toronto, from April 3 to April 6. The course is under the auspices of the General Practitioner Section of the Ontario Medical Association.

The Medical Alumni Association has announced plans to combine its fall post-graduate course with that of the Ontario Medical Association.

* * *

On the evening of March 9, the Medical Alumni Association presented a Round-table Discussion on General Practice which was attended by the final year medical students and the interns of hospitals in Toronto. Seven doctors in practice in Ontario were in attendance—Dr. Agnes Jamieson of Minden, Dr. W. . Caldwell of Brampton and Drs. H. Sullivan, J. A. Patterson, G. Sinclair, F. Preston and H. G. Hall of Toronto. They discussed such aspects of the subject as, "Women in General Practice,' "Practice in An Average-sized Town," "General Practice in the City," "Group Practice," "Industrial Medicine," and "The Experience of a Recent Graduate." Dr. V. F. Stock was chairman of the meeting. After a most interesting and worthwhile discussion, refreshments were served and the students had the opportunity of meeting the individuals on the panel.

R. L. SMITH

PROPOSED REVISION OF THE MEDICAL SOCIETY CONSTITUTION

The retiring Medical Society Constitution Committee has announced its proposed revision of the Medical Society Constitution. Along with several minor changes, three major changes are suggested.

First, it is felt that the Vice-President should assume the duties of Social Co-ordinator, organizing the Meds At-Home as in the past, and, in addition, linking the Society Executive with the Panacea and the Daffydil Committees. With this reorganization, the Daffydil Chairman would no longer hold a voting position on the Medical Society Executive.

Second, it is proposed that the Chairman of the Medical Arts and Letters Club become known as the Chairman of Medical Arts and Letters, and that a number of small intra-faculty groups be formed for those undergraduates who are particularly interested in such things as the Medical Glee Club, music appreciation, and art. This proposal would eliminate the voting position, now held on the Medical Society Executive, by the Medical Glee Club Director.

Third, with the dissolution of the University of Toronto Ex-Service Committee, and the National Committee of Student Veterans, it is suggested that an Ex-Service Representative be no longer a voting member of the Executive Council. The Committee believes that, as D.V.A. benefits have now passed their peak, any problems which will arise in the future are likely to be individual problems, best handled by the undergraduate himself.

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1. Marbach, A. H.: Am. J. Obst. & Gynec. 55: 511, 1948.

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1. Carliner, P. E., Radman, H. M., and Gay, L. H.: Science, 110:215 (Aug. 26/49). 2. Gay, L. H., and Carliner, P. E.: The Prevention and Treatment of Motion Sickness. Bull, Johns Hopkins Hosp., May 1949. 3. Beeler, J. W., Tillisch, J. H., and Popp, W. C.: Proc. Staff Meet. Mayo Clinic (Sept. 14/49).

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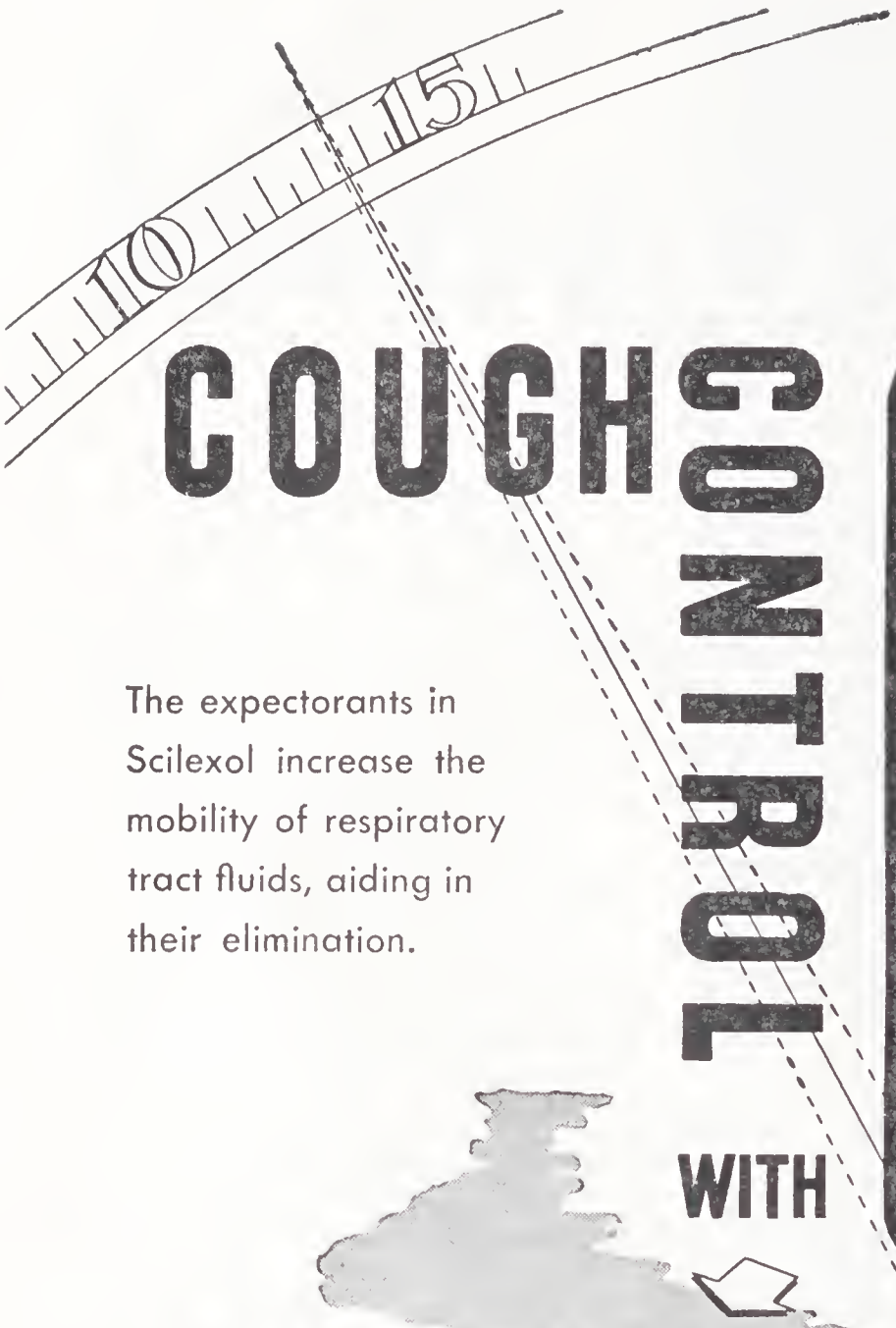

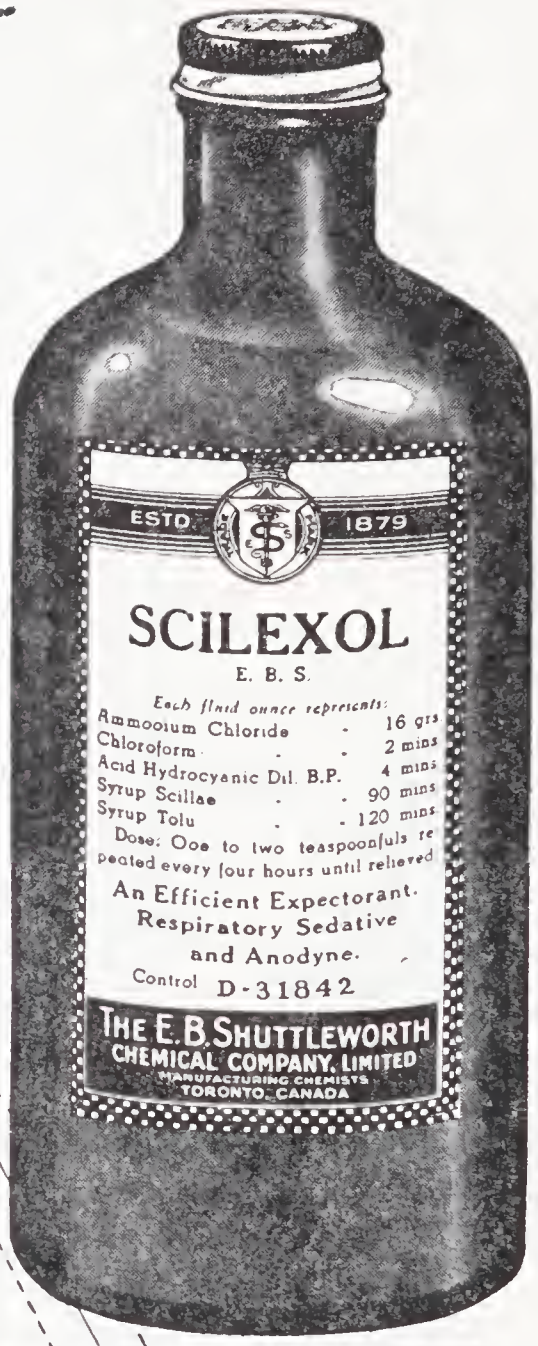
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